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VOLUME 40 NUMBER 2

AMERICAN JOURNAL

OF

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AUGUST, 1930

PUBLISHED MONTHLY BY AMERICAN MEDICAL ASSOCIATION, 535 NORTH DEARBORN STREET, CHICAGO, ILLINOIS. ANNUAL SUBSCRIPTION, $8.00

Entered as Second-Class Matter, January 4, 1911, at the Postoffice at Chicago, Illinois, Under Act of Congress of March 3, 1879. Acceptance for mailing at special rate of postage provided for in Section 1103, Act of October 3, 1917, authorized on June 14, 1918.

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American Journal of Diseases of Children

VOLUME 40 AUGUST, 1930 NUMBER 2

ENCEPHALOGRAPHY IN CASES WITH FIXED LESIONS OF THE BRAIN *

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BOSTON

Encephalography involves the removal of cerebrospinal fluid and its replacement by air. This is definitely a formidable procedure and is probably uniformly followed by a meningeal reaction. In this paper we report our experience with this admittedly severe method of study as it was applied to a group of children with supposedly fixed lesions of the central nervous system. We believe that the method reveals information of great value, and that as a result treatment can be carried out more promptly and more adequately in many cases.

It is unnecessary to discuss the literature in any detail, since Pancoast and Fay summarized it in a recent article.[1] The daring and effective investigations of Dandy are of course fundamental.

Two major methods of introducing air into the spaces usually occupied by fluid have been used; the introduction into the ventricles by direct puncture and the introduction through a needle in the lumbar subarachnoid space. X-ray films taken after direct puncture of the ventricles are always called ventriculograms. After lumbar puncture the air is likely to reach the general subarachnoid space as well as the ventricles, and the resulting film is often called an encephalogram. In addition, certain Hellenic enthusiasts have evolved the world pneumorrhachicentesis for the procedure. In this paper we follow Pancoast and Fay in referring to encephalograms.

*Submitted for publication, Feb. 24, 1930.

*Read at the Forty-Second Annual Meeting of the American Pediatric Society, Montreal, June 18, 1930.

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*The work represented by this paper was rendered possible by a grant from the Julius Rosenwald Fund of Chicago.

1. Pancoast, H. K., and Fay, Temple: Encephalography: Roentgenological and Clinical Considerations for its Use, Am. J. Roentgenol. **21**:421, 1929.

The neurologic material in a children's hospital can be divided fairly satisfactorily into three groups. First, there are the children suffering from active or progressive disease. On the whole, this group is dealt with enthusiastically and intelligently. Meningitis, tumor and the various well demarcated syndromes are typical members of this group.

Second, children afflicted with prenatal defects, such as mongolism, spina bifida and the like, are regarded with well justified pessimism.

Third, there is a group of children whose nervous systems have been attacked by any one of various agents, of which trauma and infection are the most important, that have left anatomic defects or physiologic perversions. This group, which is very large, can be subdivided into two groups: (1) children with poliomyelitis and (2) those with cerebral damage. It is with the final group that this paper is chiefly concerned.

It can be demonstrated, we believe, that trauma and infection in general are grossly nonselective agents as far as the brain is concerned. We realize, of course, that certain epidemic diseases leave fairly characteristic sequelae, but the end-product after trauma or infection is unlikely to be a conventional syndrome. We believe that any adequate study of these cases should establish three points: (1) the anatomic situation, (2) the physiologic residue and (3) a logical educational program. Not one of these obvious requirements is adequately covered by the ordinary method of medical investigation of the group we discuss, and we believe that a confession of previous failure and a search for better methods are necessary.

In making the assertion that previous methods have failed to establish anatomic facts during life, we are on safe ground. Routine physical examination, in early childhood at least, reveals the size of the head, the presence of gross motor disturbances which have some relation to a relatively small portion of the central nervous system and a few other bits of data which, in extreme cases, justify complete pessimism. Beyond this, definite information is hard to get by this method.

Lumbar puncture and roentgenograms of the skull in most cases are troublesome gestures of predictable futility. Wassermann reactions are almost uniformly negative, though of course they should always be performed. The net result of the conventional "hospital observation" is negative and rather exasperatingly negative, since it does not reveal or rule out structural changes which may be present. The obvious limitations of the conventional methods of study keep parents and physicians wondering whether exploration might reveal a situation in which radical surgical attack might be justified.

This attitude makes it extremely difficult to establish a logical educational régime, since the certainty which follows a conclusion based on adequate information is lacking. We sympathize entirely with parents

who regard the diagnoses of feeblemindedness, epilepsy or severe and unmanageable deformities as inadmissable until every reasonable effort has been made to establish all facts. The question as to whether an admittedly formidable procedure such as encephalography is reasonable is dependent, it seems to us, on the answers to the following questions:

1. Is definite diagnosis possible without it?
2. Is the procedure likely to clarify the situation, and to what extent?
3. Is there any likelihood that conditions will be made worse?
4. Is the mortality serious?
5. How severe is the reaction?

1. The answer to the first question depends on what is regarded as a definite diagnosis. We grant at once that feeblemindedness, epilepsy and cerebral palsy are often easy to identify and that, on the whole, children with these disorders usually follow a discouraging course, ending in educational and social failure. We are not willing, however, to admit that the use of any one of these names implies accurate knowledge of the anatomic situation or of the physiologic assets. Clearly, it is entirely possible to predict with certainty the course of events in many extreme cases, and we agree that encephalography should be restricted to cases in which there is doubt as to the anatomic situation. Our present attitude is that good judgment of slight cases requires some information on the situation in the more severe ones.

2. The second question can be answered categorically. We are all agreed that approximately 50 per cent of the encephalograms in a consecutive series of nearly 200 cases have revealed definite evidence of distortion or enlargement of the ventricles or enlargement of the subarachnoid spaces suggesting cerebral atrophy. As we shall point out later, there are a number of points on which further information is highly desirable. Various details of interpretation should be viewed with obstinate skepticism. Any one who has followed the shift of opinion in regard to interpretation of roentgenograms of the thymus gland must recognize the possibility of errors of interpretation when a highly vascular organ is studied by practically instantaneous exposure. We know how much change in brain bulk can be produced by circulatory disturbances and by chemical means, and we are ready to admit that our conclusions are by no means absolute.

3. There appears to be no likelihood of making matters worse. On the whole we have gained a tentative impression that after the subsidence of the reaction convulsions are less frequent and less severe for a period, and we have never observed any unexpected mental deterioration or increase of motor disability.

4. One patient died after encephalography was performed. The history follows.

A male infant, aged 15 months, had done well till 6 months of age. At that time he had convulsions, which had recurred at intervals since. Without any excessive drug therapy, the child had become more and more lethargic. When he entered the hospital he was stuporous and had nystagmus and strabismus; the limbs showed weakness, but no clearly defined changes in reflexes. The eyegrounds were normal.

Fig. 1.—Encephalogram in fatal case.

A lumbar puncture was made, and 2 cc. of clear fluid obtained; 8 cells were found, and the pressure was low. Nothing abnormal was found on detailed study.

The following day, 35 cc. of fluid was removed and 35 cc. of air injected. Examination revealed 500 cells, of which 75 per cent were lymphocytes, and an increase of globulin.

Two days later presumably traumatic blood interfered with the interpretation of the observations, but another puncture four days after the injection of air showed 80 cells, 80 per cent lymphocytes and positive globulin. Cultures were sterile. Wassermann reactions of the blood and the spinal fluid were negative.

Tuberculin tests with 1:1000, 1:200 and 1:100 concentrations gave negative results. The encephalograms showed large ventricles. The chart showed no particular reaction, no temperature over 100 F. being recorded.

Without warning the child suddenly died just before we planned to discharge him on the nineteenth day after encephalography.

The autopsy report showed localized gliosis of the cerebrum on the right, pachymeningitis with slight intradural hemorrhage and edema of the meninges.

COMMENT

The contrast between the first fluid and that obtained at the time of the injection of air is obviously not dependent on the irritant effect of the air. Any such reaction to the withdrawal of 2 cc. of fluid twenty-

*Changes in the Spinal Fluid After Encephalography in Five Typical Cases**

	Before						After					
Hospital No.	Color	Globulin	Sugar	Cells	Polymorphonuclears	Lymphocytes	Time, Hrs.	Color	Globulin	Sugar	Cells	Polymorphonuclears	Lymphocytes
12824	Clear	0	+	5	0	5	24	Clear	+	+	16	12	4
							36	Clear	+	+	18	14	4
							48	Clear	+	+	8	..	8
13874s	Clear	0	+	2	0	2	16	Clear	+	+	980	85%	15%
							24	Clear	+	+	476	80%	20%
							48	Clear	+	+	200	70%	30%
							72	Clear	+	+	85	60%	40%
13007s	Clear	0	+	0	0	0	24	Cloudy	+	+	1,000	90%	10%
							48	Clear	+	+	150	60%	40%
							72	Clear	+	+	85	50%	50%
13990	Clear	0	+	6	0	6	24	Clear	+	+	145	80%	20%
							48	Clear(?)	+	+	138	75%	25%
							72	Clear	+	+	140	50%	50%
							96	Clear	+	+	100	50%	50%
							120	Clear	+	+	90	50%	50%
13446	Clear	0	+	1	0	1	12	Cloudy	+	+	1,500	98%	2%
							36	Clear	+	+	48	58%	42%
							48	Clear	+	+	30	50%	50%

* Cultures of the spinal fluid were negative in all cases.

four hours before is outside of our experience. It seems possible that the injection of air, which of course involves practically complete emptying of all the cerebrospinal fluid spaces, forced fluid from the cortical subarachnoid spaces. It is only fair, however, to record this as a case of death subsequent to encephalography.

5. If death is rare, reaction is the rule. During injection, pallor sweating and vomiting are common, and rather alarming collapse is not rare. Beginning a few hours after the procedure and lasting in some cases for several days, febrile reactions are common. During this stage a stiff neck and Kernig's sign, suggest meningeal irritation, and this suggestion is supported by the following reports on fluids obtained by postoperative lumbar punctures.

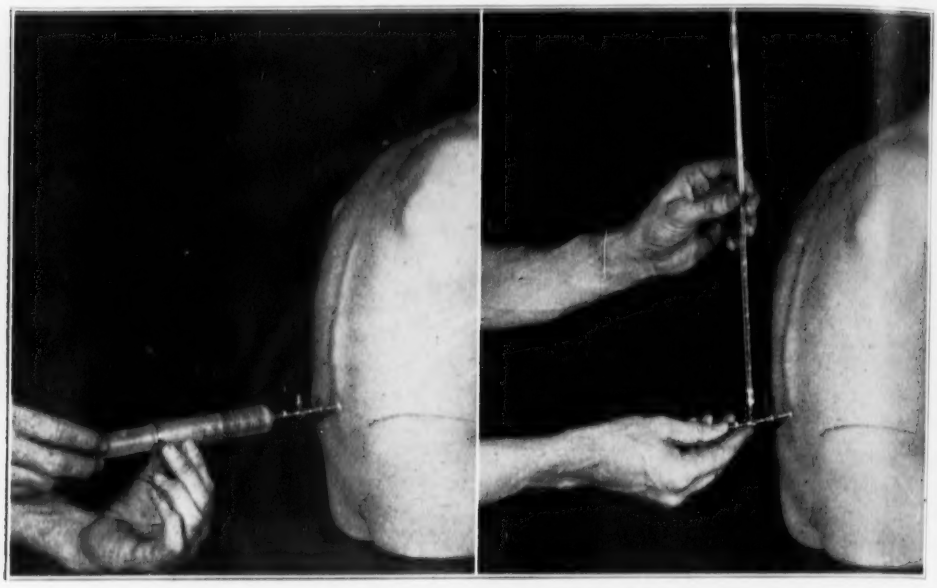
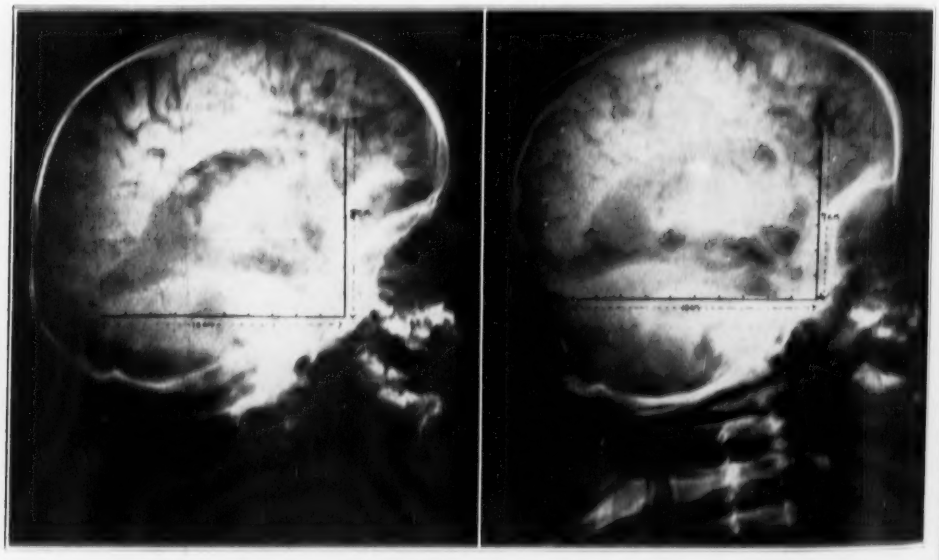


Fig. 2.—Technic of the injection of air; the iliac crests are marked. The manometer shown was devised by Dr. J. B. Ayer and is manufactured by Codman and Shurtleff, Boston.



A B

Fig. 3.—*A* shows the lateral view with the child quiet; *B*, lateral view during jugular compression involving marked cyanosis; no change in ventricular shadows, but obvious diminution in depth after compression; graduations are marked in centimeters on film.

A B

Fig. 4.—absence of change of size or contour on jugular pressure. *A*, immediately after injection: asymmetry of ventricles in epileptic child with left hemiparesis. *B*, twenty-four hours later: in spite of obvious changes in ventricles no evidence of discomfort; this is an extreme but by no means a unique change in size and contour.

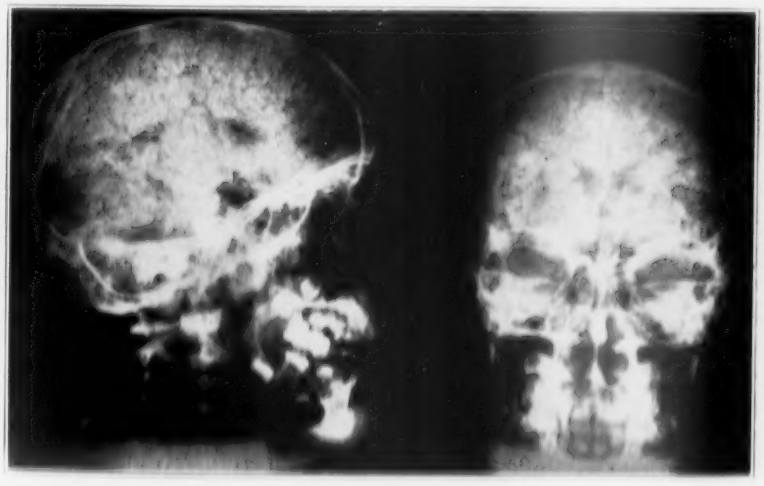


Fig. 5.—Normal encephalogram.

Fig. 6.—The patient, aged 8 years and 7 months, was admitted to the hospital on account of convulsive attacks of three months' duration; the only previous illness was severe whooping cough at the age of 5. The films show calcareous masses; the close proximity of the normal ventricles practically rules out expanding lesions and suggests the possibility that these calcareous masses may be the result of hemorrhage during the whooping cough.

Fig. 7.—The patient, aged 26 months, was always backward without any particular symptoms. The films show marked symmetrical dilatation of the ventricles without excessive air in the subarachnoid space.

If after frank acknowledgment of the danger and discomfort of the procedure the decision to consider it is reached, one almost absolute contraindication should be reviewed. If the intracranial pressure is elevated, encephalography is so dangerous as to be practically inadmissable. We respect Pancoast and Fay's routine establishment of pressure levels. However, we have become skeptical of manometric values in children and prefer to be guided by eyeground changes, cracked pot percussion notes, etc. Obviously, direct ventriculography through a trephine opening or through the fontanel is a procedure with a distinct and different series of indications.

TECHNIC

The Technic of Injection.—We believe that it pays abundantly to make sure that the child is not hurt or alarmed. General anesthesia by ether or by gas and oxygen is satisfactory for the operator, but raises difficulties in the x-ray room on account of deep and irregular respirations or vomiting. The intravenous injection of iso-amyl-ethyl barbituric acid is effective and was used in many of our cases, but it seems clear that absolute unconsciousness is neither necessary nor entirely advantageous. Frequently repeated small doses of morphine until extreme drowsiness supervenes followed by careful local anesthesia is the least alarming and perhaps the best method.

The selection of a needle and the technic of its introduction need not be reviewed, since no one who is not entirely familiar with the procedure of lumbar puncture should consider encephalography. We do our puncture with the child sitting up. Pancoast and Fay and various others use two needles; one of these is used for drainage and the introduction of air, while the other remains connected with a mercury manometer. We have used the manometer devised by Ayer with a three-way stop-cock and see no advantage in the second puncture. In children the chances of trauma and consequent bleeding are great with one needle, and it would take a demonstration of considerable merit to persuade us to double our risk of trauma.

We have always observed the pressure immediately after the introduction of the needle and at intervals during the whole procedure. We try to keep the pressure throughout at a lower level than at the beginning and to leave it at 100 mm. of fluid or lower. We observe the manometric readings, but in children we find it very difficult to believe that absolute figures are particularly important.

The fluid is allowed to drain slowly until 5 cc. is withdrawn; 5 cc. of air is then introduced by gentle pressure from a glass syringe. Pressure is checked and the process is repeated. If the flow of fluid is interrupted, rotation of the head in various directions often releases fluid from dependent portions of the ventricular system. The general rule we follow is to stay within reasonable distance of a volume by volume replacement and watch the pressure so that it is always below the initial reading. Varying amounts of air are needed. A glance at our roentgenograms will demonstrate the futility of setting up standards before injection. One rather mystifying observation is that 20 cc. may apparently fill a large ventricular system while 50 cc. may be introduced into a head of the same size with small ventricles. The difference is presumably accounted for by different amounts in the subarachnoid spaces, though this theory is not always

Fig. 8.—The patient was 5 years and 9 months of age. A seven months' pregnancy had been followed by severe and prolonged sepsis including osteomyelitis and erysipelas with the result that the child was very ill for at least six weeks after birth; it had always been retarded and had frequent attacks of what was apparently petit mal. The films show definite asymmetry and enlargement of the ventricles.

Fig. 9.—The patient, aged 4 years and 6 months, admitted to the hospital on account of convulsive attacks, spasticity and idiocy. The child was definitely well until 18 months of age, when she had a severe attack of pertussis, sudden convulsions, subsequent paralysis and mental impairment. The films show an extraordinarily symmetrical dilatation of the ventricles in a relatively small head; this represents widespread atrophy as a known consequence of whooping cough, presumably a definite encephalitic process due to pertussis.

Fig. 10.—In this patient, aged 5 months, a diagnosis of mongolism was definitely supported by the usual evidence. The films show slightly dilated ventricles but the main thing is the extraordinary depth of the subarachnoid space and apparently widespread atrophy in the frontal region.

Fig. 11.—A patient, aged 1 year, had persistent convulsions and backwardness; all the sutures were closed. The films show marked symmetrical dilatation of both ventricles.

Fig. 12.—The patient, aged 20 months, was admitted to the hospital on account of retardation both mental and physical. There was a clear history of birth injury with definite treatment therefor. The films show marked dilatation of both ventricles, probably symmetrical, although the anteroposterior view is not exactly in line; there is also a considerable amount of air in the subarachnoid space, especially on the right side.

Fig. 13.—A patient, aged 19 months, at 1 month had a severe attack of pertussis with internal stabismus; apparently normal development took place until 18 months of age when the child became stuporous and unable to use the arms or legs. The films show marked dilatation of the ventricles. An old choroiditis suggested that the pathologic condition preceded recent symptoms.

supported by the appearance of the films. We have not attempted to squeeze the last drops of cerebrospinal fluid by jugular compression during the procedure, though this method may be logical.

During the injection the properly prepared child is usually quiet, the pulse stays reasonably steady, and the color remains good. Pallor, irregular respiration, profuse sweating and vomiting are, however, not unusual. In the presence of such symptoms, we proceed cautiously and with some anxiety. We have never seen a catastrophe during or immediately after injection.

At the completion of the injection, the child is taken to the x-ray room on a stretcher. A sterile puncture needle is kept at hand, not only in the immediately postoperative period, but for twenty-four hours thereafter. We have felt sure that occasionally we have been able to intervene to advantage by letting off air or fluid under pressure. We have, indeed, a definite impression that the reintroduction of a needle after roentgenograms are taken may become part of our routine.

When the child reaches the x-ray room, the following method is pursued. The exposures are made according to the usual procedures for ventriculography. We have used an ordinary Potter-Bucky diaphragm on a horizontal table exclusively. With the patient in the prone position, we take right and left lateral stereoscopic films, shifting lengthwise to the patient at a distance of 25 inches (63.5 cm.). The patient is then placed on his back, face up, for the anteroposterior view. The head is turned from side to side beginning with an angle of about 60 degrees, but gradually diminishing the arc till the face is directly up. This is to equalize the remaining fluid and air in the ventricles. A single straight anteroposterior exposure is then made. After this the patient is turned face down, and a posteroanterior film is taken which outlines the posterior horns. Care must be taken to have the patient exactly centered.

We have emphasized the importance of proper delineation of the ventricular system, because we feel that the information gained is definite, since we think we know what normal ventricles look like. This does not mean, however, that we disregard the air in the subarachnoid space, but as there is evidently a considerable variation in the amount that may be present under normal conditions, caution must be exercised in its interpretation.

It is evident, of course, that the technic described is less elaborate than that used in certain clinics where most of the patients are adults. We believe that, after proper preparation of the patient, good films can be obtained in this way. In the early months of our study, we found that poor films were obtained regardless of position unless adequate amounts of an efficient narcotic or anesthetic had been used.

INTERPRETATION

We assume that the shadow of the ventricle is slightly larger than the ventricle itself. We have checked this impression by making exposures with a distant tube. The error seems to us unimportant. We also assume that no great variation occurs with transient changes of pressure.

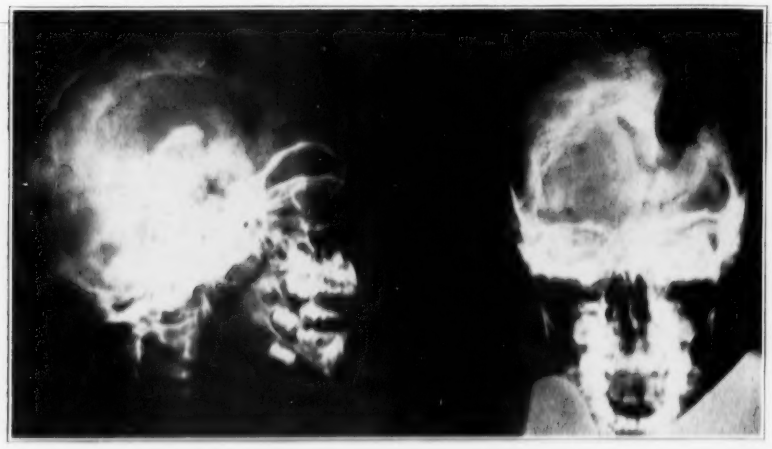


Fig. 14.—The patient, aged *2* years and 11 months, was admitted to the hospital on account of mental retardation, right hemiplegia and right-sided convulsions; on the third day of life the child bled profusely from cord stump and mouth and little hope for his life was entertained. The films show a dilated left ventricle and marked displacement to that side.

Fig. 15.—In this patient, aged *3* years and 10 months, disability apparently dated from severe convulsions at 10 months of age which persisted at intervals for three years. At the time of entrance to the hospital the child was backward, unable to walk and having occasional convulsions. The films show marked asymmetry of the ventricles, the right being the larger, with displacement toward the right side.

Fig. 16.—The patient, aged 4 years, had a cleancut history of an infectious process at 13 months with severe convulsions. Left hemiplegis which occurred at that time persisted. There were recurrent convulsions without great mental defect; films show marked dilatation of the right ventricle with definite displacement to the right, indicating massive atrophy of that side of the brain.

Fig. 17.—The patient, aged 6 years, had a cleancut history of birth injury with positive lumbar puncture observations at the time; convulsions and feeble-mindedness had been present since. On the whole, there were more signs of paralysis on the right. The films show definite asymmetry of the ventricles, both of which are enlarged, and displacement toward the side with the larger ventricle.

Fig. 18.—The patient, aged 10 years, had had right hemiparesis from infancy and occasional convulsions, largely on the right side. He had reached fourth grade, but on the whole mental deterioration and emotional instability was evident for months before entrance. The films show the ventricles to be markedly enlarged and a large distorted posterior horn on the left; 150 cc. of fluid was removed and the same amount of air injected.

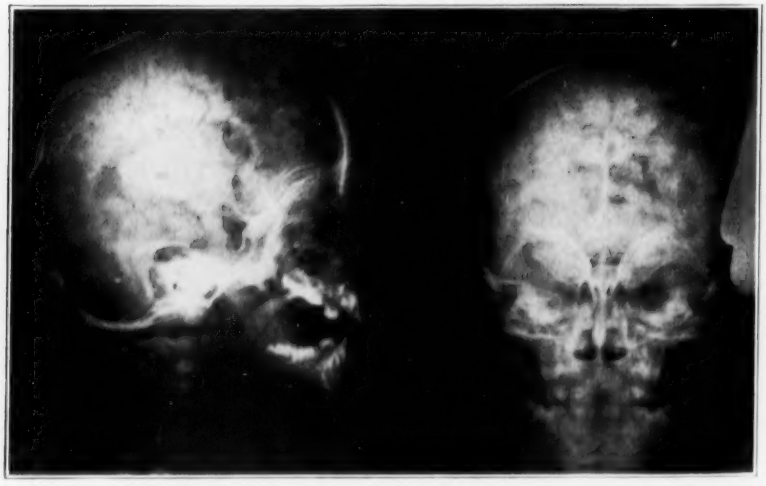


Fig. 19.—The patient, aged 17 months, was a frank microcephalic idiot without any definite etiology. The films show a definite increase in the depth of the subarachnoid space particularly in the frontal region, and slightly large ventricles.

We have checked this assumption by jugular pressure (fig. 3), taking films before and during such pressure. We see no reason to believe that transient variations in pressure confuse the situation to any serious extent. It is interesting, though slightly irrelevant for the moment, to observe that films taken a day or two after the injection of air may show definite increase of size of the ventricles (fig. 4). This we assume to be due to the inflammatory reaction described.

If we assume, with some confidence, that standards of size and shape of the ventricles exist, though we are not clear that we have entirely adequate information on this point, we are less sure of our standards concerning the subarachnoid spaces. However, we now have a good deal of data and present a few striking cases of deviation from the usual.

A "normal" film shows symmetrical ventricles and even markings over the cortex. Figure 5 illustrates our ideas of a normal film. We recognize the fact that other observers might suggest that the subarachnoid space is wider than normal, but we are not convinced that the shadows are not within normal limits. Later we show films that reveal what we regard as definitely enlarged subarachnoid spaces.

We have divided the films showing unusual distribution of air into four groups:

1. *Reasonably Symmetrical Dilatation of Ventricles.*—In general, we regard the dilatation as due to a deficit of brain tissue rather than as hydrocephalus from obstruction or lack of balance between formation and absorption of fluid.

2. *Marked Asymmetry of Ventricles, Presumably from Unilateral Atrophy.*—It will be noted that in general the displacement of the intracranial contents is toward rather than away from the enlarged ventricle. This is, of course, a vital point if tumor is one of the possibilities.

3. *Evidence Suggesting Deepened Subarachnoid Spaces Dependent on Cortical Atrophy.*—We are frankly dubious about some of these cases, but present them for what they are worth.

4. *Absence of Air in Ventricles.*—If no other evidence of block exists, we regard failure of air to enter the ventricles as due to some unknown factor or to faulty technic. With increasing experience, we have few such results. Obviously, such films add to, rather than decrease, the complexity of diagnosis.

CONCLUSIONS

Although encephalography is admittedly a severe and probably a dangerous procedure, we know of no case in which its use has led to an aggravation of previously existing disorders.

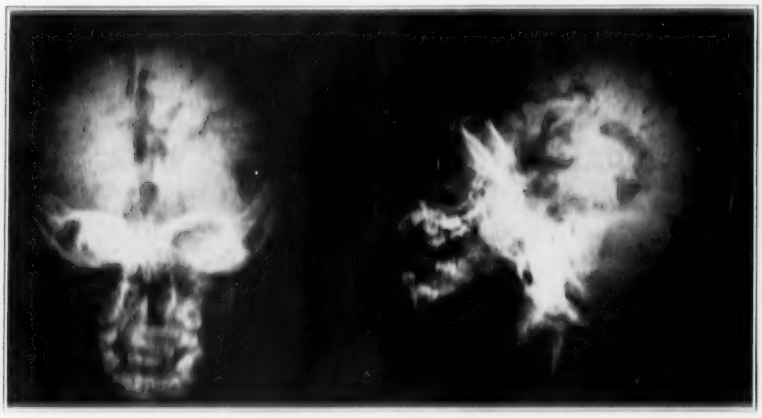


Fig. 20.—The patient, aged 14 months, was admitted to the hospital on account of feeblemindedness. The films show small but markedly distorted ventricles and a marked increase of depth of the subarachnoid space almost certainly representing widespread atrophy.

Fig. 21.—The patient, aged 3 years and 8 months, was admitted to the hospital on account of left hemiplegia and convulsions dating from birth. The films show little or no dilatation of the ventricles with slight displacement to the right.

Fig. 22.—The patient, aged 22 months, was admitted to the hospital on account of convulsions and failure to develop mentally. No cleanent cause was made out although the child had a good deal of infection during early infancy; it is possible that this represented postmeasles encephalitis. The films show symmetrical ventricles without distortion; there appears to be a good deal more air than usual in the subarachnoid space, and it is possible that this represents cortical atrophy.

Fig. 23.—The patient, aged 3 years and 6 months, was treated at the Children's Hospital at 18 months for definite lead poisoning with recovery of lead and definite history of ingestion of lead by chewing paint. At the time of acute disease, marked edema of the brain was demonstrated. The child subsequently had convulsions, hemiplegia, optic atrophy and was mentally retarded. The films show definite distortion and enlargement of the ventricles with widespread atrophy of the cortex on the right; the whole situation justifies the diagnosis of widespread brain atrophy following lead encephalitis.

The conventional diagnoses of feeblemindedness, epilepsy and cerebral palsy do not define the anatomic defect or the physiologic residue, and give no suggestion for adequate educational programs. In our hands the traditional period of hospital observation, with investigation of the blood and the spinal fluid and inspection of ordinary x-ray films of the skull, has given little information of definite value.

Encephalograms, properly taken and intelligently interpreted, give definite information of positive value in at least one half of properly selected cases. In the remainder, negative facts of importance can be established. We believe that encephalography should be used before final judgment is passed on the future of children severely handicapped by fixed cerebral lesions, unless other less severe methods are demonstrably adequate.

We are, of course, unable and unwilling to make diagnostic or prognostic decisions on the basis of encephalograms alone.

GIANT CELLS IN INFLAMMATIONS OF THE LUNG IN CHILDREN *

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CLEVELAND

"Giant cell" pneumonia has received occasional attention since the first report of Buhl.[1] Among others, Hecht,[2] Aufrecht,[3] Friedländer [4] and Karsner and Meyers [5] have reported cases and discussed the origin and significance of the cells. In the course of routine autopsy examination of children, certain facts and interpretations have become evident. Since these conclusions are in contrast to the accepted German opinions, it seems desirable to record them.

For purposes of this discussion a giant cell is defined as a protoplasmic mass with two or more nuclei. With this criterion, we have encountered giant cells in early acute bronchopneumonia, in late postinfectious bronchopneumonia, in the alveoli about areas of acute bronchopneumonia, in the type of lesion designated as "pneumonic desquamativ" and in pneumonia alba. In this paper we shall record briefly the clinical and autopsy observations in five typical cases, and shall discuss the types of cells and their origin and significance.

REPORT OF CASES

CASE 1.—A white boy, aged 6 months, was admitted to the Babies' and Children's Hospital because of persistent fever and cough of one week's duration. Three weeks before, while at home, he had a respiratory infection, probably pneumonia, of one week's duration, with a relapse one week later. He had been

* Submitted for publication, Feb. 18, 1930.

* From the Institute of Pathology and the Babies' and Children's Hospital, Western Reserve University.

1. Buhl, L., quoted by Karsner, H. T., and Meyers, A. E.: "Giant-Cell Pneumonia," Arch. Int. Med. **11**:534 (May) 1913.

2. Hecht, V.: Die Riesenzellenpneumonie im Kindesalter, Beitr. z. path. Anat. u. z. allg. Path. **38**:263, 1910.

3. Aufrecht, E.: Die Lungenentzündung, in Nothnagel: Spezielle Pathologie und Therapie, Vienna, Alfred Hölder, 1894, vol. 14, part 1, pp. 275 and 894.

4. Friedländer, C.: Experimentelle Untersuchungen über chronische Pneumonie und Lungenschwindsucht, Arch. f. path. Anat. **68**:325, 1876.

5. Karsner, H. T., and Meyers, A. E.: Giant Cell-Pneumonia, Arch. Int. Med. **11**:534 (May) 1913.

unable to move the legs or arms since birth, and the neurologic observations plus a history of a sixteen hour labor with forceps supported a diagnosis of injury at birth. Examination at admission showed a poorly nourished and developed infant. The percussion note was hyperresonant on the left side and impaired on the right with dulness posteriorly. There were no rales. The laboratory observations were: urinalysis, negative; white blood cells, 35,800; hemoglobin, 70 per cent; Wassermann reaction, negative. X-ray pictures of the chest showed marked infiltration about the right hilus with displacement of the heart and trachea to the right. The respiratory infection became more severe, and death

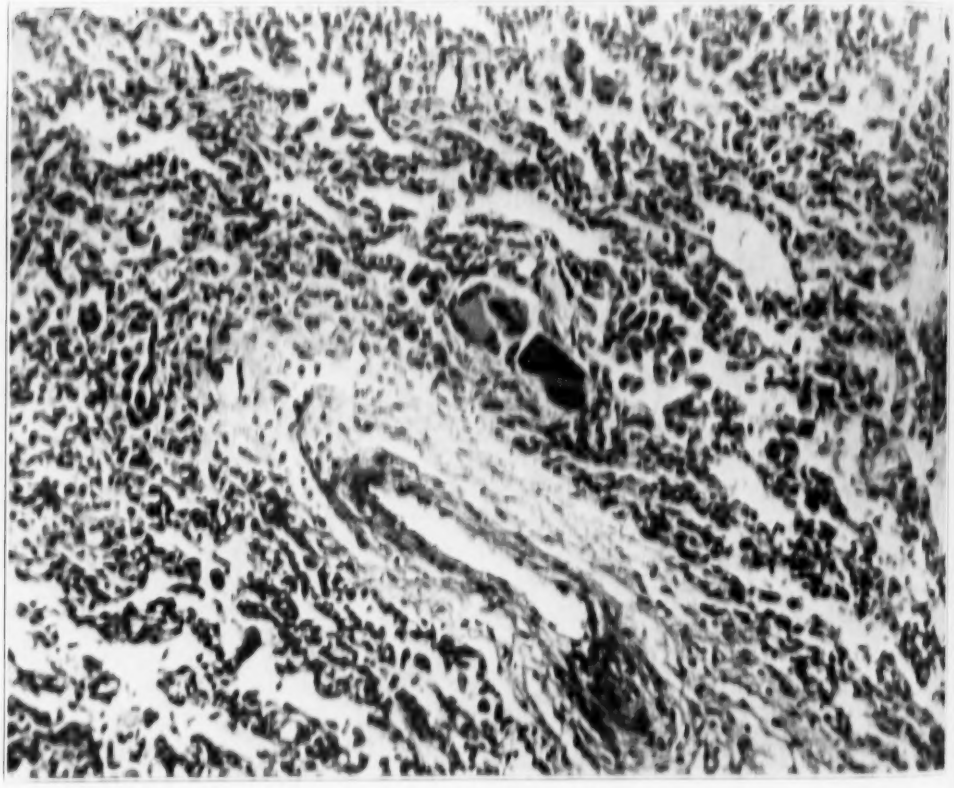

Fig. 1 (case 1).—Two Langhans' giant cells in an alveolus. Note the thick alveolar walls, desquamation and lymphoid infiltration; × 190.

occurred on the twenty-sixth hospital day. The clinical diagnosis was: bronchopneumonia; bilateral acute suppurative otitis media; trigocephaly; injury at birth.

Autopsy performed by Dr. W. W. Herrmann four and one-half hours after death, showed: bilateral subacute bronchopneumonia; acute suppurative bronchitis; acute hyperplastic lymphadenitis of the tracheobronchial nodes; bilateral acute suppurative otitis media; progressive muscular atrophy, infantile type; internal hydrocephalus, and cloudy swelling of the parenchymatous viscera.

The lungs were small, partially collapsed and dark red and cut with increased resistance. The pleura was normal. Throughout all the lobes were numerous

nonconfluent, reddish-gray, elevated, firm nodules, from 2 to 4 mm. in diameter. In the right upper lobe the nodules were firmer and yellow. The small and medium sized bronchi were filled with purulent material. The small bronchi were prominent and surrounded by a zone of dense, reddish-gray tissue. Microscopically, the majority of alveoli were filled with an exudate composed of large mononuclears, polymorphonuclears and lymphocytes with little fibrin. In some alveoli, typical Langhans' giant cells were present (fig. 1). In others, there were necrotic masses of homogeneous granular débris with entrapped pyknotic nuclei

Fig. 2 (case 1).—A necrotic mass of alveolar exudate attached to the wall; × 300.

(fig. 2). There was a subacute peribronchiolitis about all of the bronchioles. In some bronchi, the epithelium was desquamated and fused into multinucleated masses (fig. 3).

It is evident that this case is similar in clinical and pathologic features with those described by Hecht[8] and Karsner and Meyers.[5] It is representative of "Riesenzellen pneumonie." Two distinct types of multinucleated cells were present with additional multinucleated necrotic

masses. Many features resembled those observed by MacCallum[6] in postmeasles bronchopneumonia or interstitial pneumonia. The pathologic changes were clearly those of a prolonged subacute process.

Case 2.—A colored boy, aged 1 year, was admitted to the Babies' and Children's Hospital with a history of convulsions for the past three days. Examination revealed many pustules in the scalp and enlargement of the cervical lymph nodes. The course continued septic, terminal signs of pulmonary infection appeared and death occurred four months after admission. The clinical diagnosis was con-

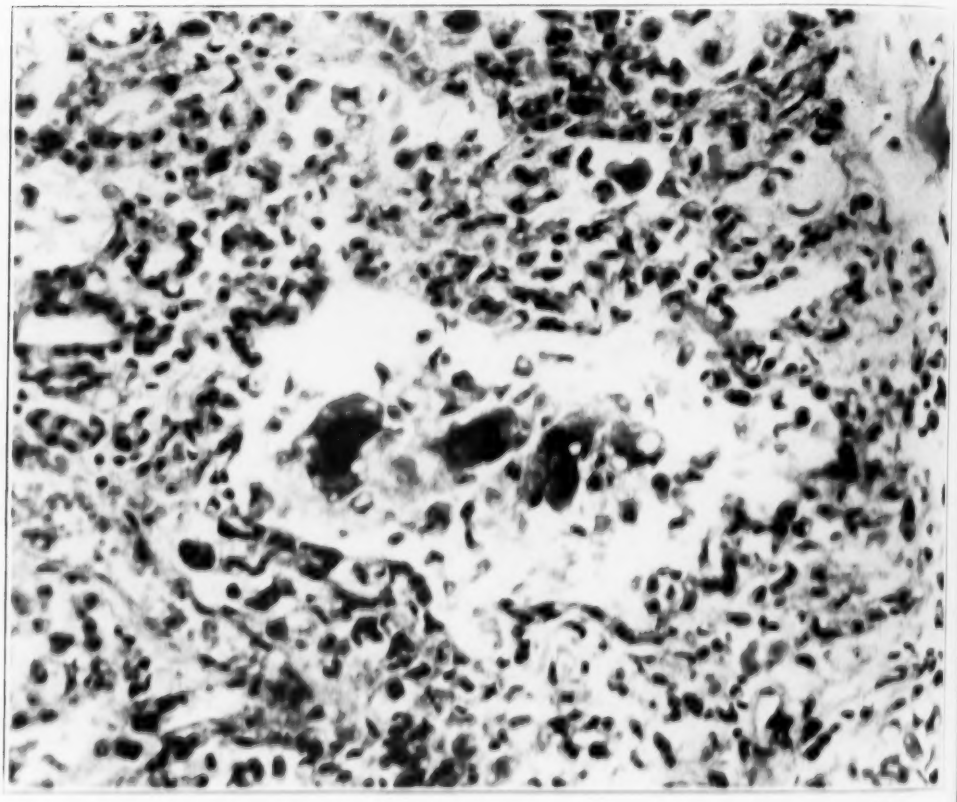

Fig. 3 (case 1).—Three giant cells formed by fusion of desquamated bronchial epithelium; × 300.

genital syphilis, furunculosis, suppurative otitis media and mastoiditis, decomposition, parenteral dyspepsia and bronchopneumonia.

Autopsy, performed by Dr. R. A. Moore three hours after death, revealed: bronchopneumonia of the upper right lung; abscess of the lung, left upper lobe; acute suppurative bronchitis, acute hyperplastic lymphadenitis of the tracheo-

6. MacCallum, W. G.: The Pathology of Pneumonia in the United States Army Camps During the Winter of 1917-1918, Monog. Rockefeller Inst. 1919, no. 10.

bronchial nodes; bilateral subacute suppurative otitis media and mastoiditis; furunculosis of the skin; acute splenic hyperplasia and cloudy swelling of the parenchymatous viscera. The pleura was normal except in an area 1 cm. in diameter over the lower lateral aspect of the left upper lobe where there were firm fibrous adhesions between the two layers. Beneath this area was a cavity 1.5 cm. in diameter filled with thick yellowish-green material, and surrounded by a fibrous wall, 2 mm. in thickness. In the upper lobe of the right lung there were numerous discrete, elevated, gray, firm nodules, from 2 to 5 mm. in diameter.

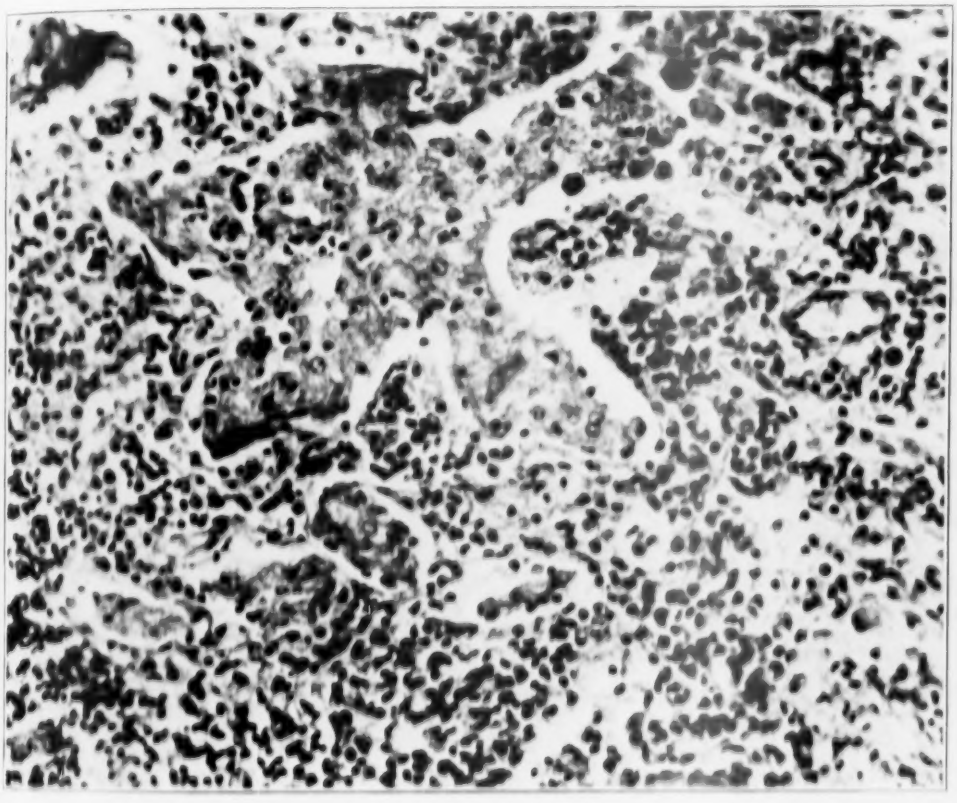

Fig. 4 (case 2).—Irregular syncitia of rich fibrinous exudate which may undergo hyalinization to resemble giant cells; × 300.

The microscopic appearance of the abscess of the lung was not remarkable. The bronchopneumonia was characterized by a large quantity of fibrin and a preponderance of lymphocytes and large mononuclears. In many instances, the fibrin filled two or more alveoli and formed large confluent masses (fig. 4). Many alveoli contained multinucleated phagocytic cells (fig. 5).

This case is representative of those in which giant cells of the endothelial type are found in association with large confluent masses of fibrin. It appears possible that the fibrinous masses, by a process of

condensation and hyalinization, may resemble the irregularly shaped giant cells of the Langhans type.

CASE 3.—A white boy, aged 6 weeks, was admitted to the Babies' and Children's Hospital because of an imperforate anus and prematurity. A colostomy was performed a few days after birth, but progress was unsatisfactory. Great difficulty was experienced in maintenance of fecal drainage, and death occurred two weeks after admission. There were no clinical signs of pulmonary disease at any time.

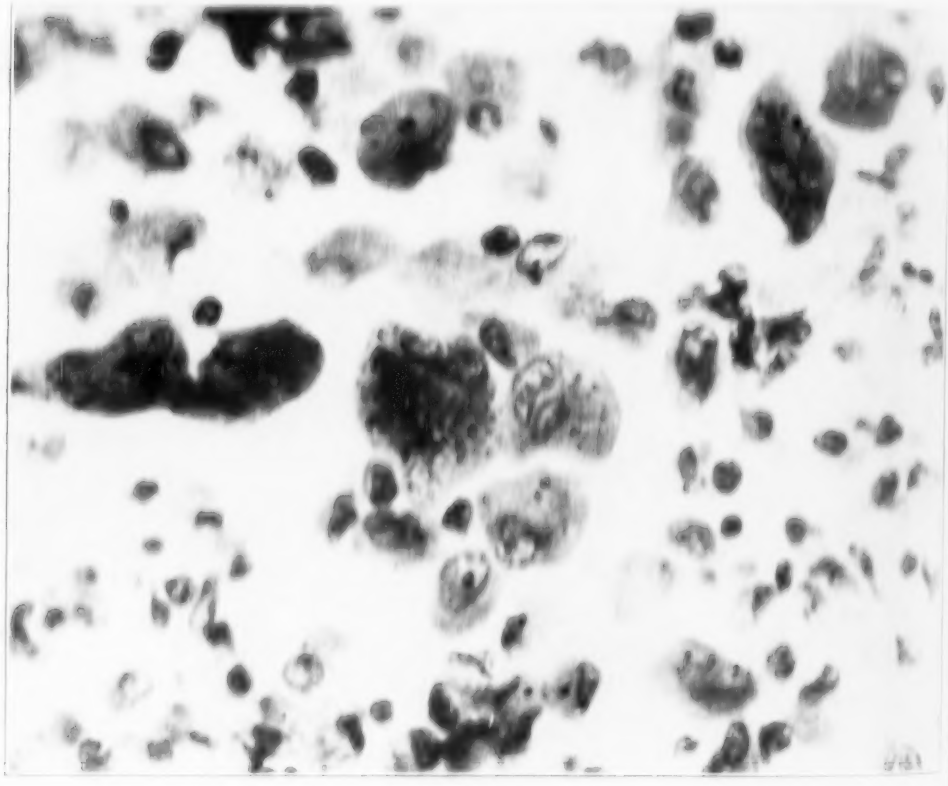

Fig. 5 (case 2).—Multinucleated cells within an alveolus containing granules of iron-bearing pigment; × 850.

Autopsy, performed by Dr. R. A. Moore four and one-half hours after death, revealed: persistent cloaca, imperforate anus, bilateral acute suppurative otitis media, pulmonary atelectasis, desquamative pneumonia, acute splenic hyperplasia, right hydronephrosis and hydro-ureter, healed colostomy wound and immaturity. Grossly, the lungs were compact, leathery and dark reddish blue. There was no gross evidence of consolidation. Microscopically, the alveolar walls were thick and the blood vessels hyperemic. The alveoli were filled with a great number of large mononuclears and a few polymorphonuclears and lymphocytes (fig. 6). Some of the large mononuclear cells were large and multinucleated (fig. 7). The bronchi were normal.

The pathologic changes in this case were the same as those described by Borst[7] and others as desquamative pneumonia. It appears unlikely that postmortem desquamation could occur as rapidly and extensively in four hours. The associated hyperemia and slight infiltration of polymorphonuclears and lymphocytes indicated an inflammatory basis.

Case 4.—A white girl, aged 1 year, was admitted to the Babies' and Children's Hospital because of vomiting and fever of five days' duration. Physical exam-

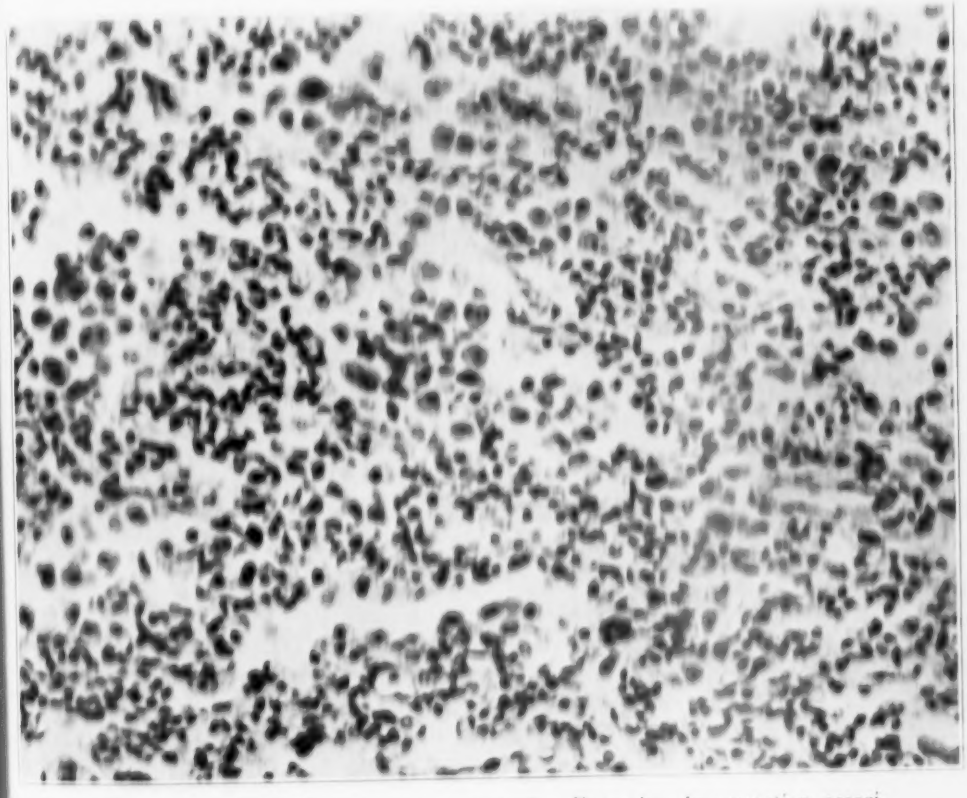

Fig. 6 (case 3).—Desquamative pneumonia. Extensive desquamation associated with hyperemia and slight lymphoid infiltration; × 110.

ination was negative, except for a general lymphadenitis and slight dulness over the upper part of the right side of the chest. The laboratory observations were: white blood cells, 10,800; hemoglobin, 50 per cent; red blood cells, 3,050,000. Signs of cerebral irritation appeared, and death occurred on the twelfth hospital day. The clinical diagnosis was: general influenzal sepsis; acute influenzal cerebral meningitis; secondary anemia.

Autopsy, performed by Dr. Herbert Reichle six hours after death, revealed: acute suppurative leptomeningitis; bilateral acute suppurative otitis media;

7. Borst, M.: Pathologische Histologie, ed. 2, Munich, J. F. Bergmann, 1926.

bronchopneumonia, upper lobe of right lung; acute splenic hyperplasia; icterus, and cloudy swelling of the parenchymatous viscera.

The lungs were normal, except the upper lobe of the right lung, which was firm and dark red. No definite areas of consolidation could be elicited. Microscopically, the alveoli of the upper lobe of the right lung were partially filled with an exudate composed of polymorphonuclears and mononuclears, with a moderate number of multinucleated cells, similar to those shown in figure 6. The blood vessels were hyperemic, and the alveolar walls were thick and edematous and infiltrated with polymorphonuclears and large mononuclears. Fibrin was absent.

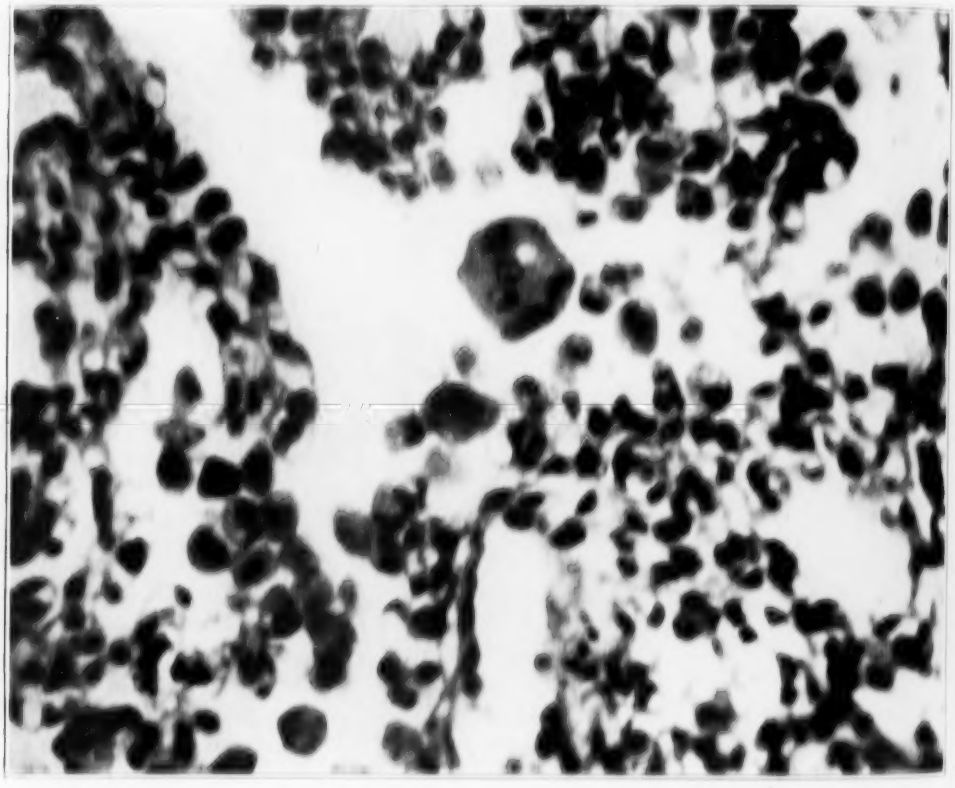

Fig. 7 (case 3).—Multinucleated cells formed from desquamated alveolar epithelium. One contains a vacuole; × 440.

The essential changes in this case are a typical early bronchopneumonia associated with marked desquamation. Many features resembled the "alveolite" recently described by Heraux.[8] In our experience, desquamation is frequent in the early stages of bronchopneumonia in children, but the presence of multinucleated cells is unusual.

8. Heraux, A.: La bronchopneumonie suraigué ou pneumonie en foyers à formes suraigués chez l'enfant, Ann. d'anat. path. **6**:595, 1929.

Case 5.—A white girl, aged 3 weeks, was admitted to the Babies' and Children's Hospital because of failure to gain. Birth occurred after a six and one-half months' gestation, with a birth weight of 2½ pounds (1,133.6 Gm.). For from three to four days after birth the skin was dark blue. On admission, there was marked emaciation and a slight icterus. Otherwise, the results of the physical examination were not remarkable. The disease followed a stormy course, characterized by dehydration and fever with occasional attacks of dyspnea and cyanosis. The laboratory observations were: hemoglobin, 40 per cent; red blood cells, 2,400,000; white blood cells, 8,600; Wassermann reaction, positive; blood cal-

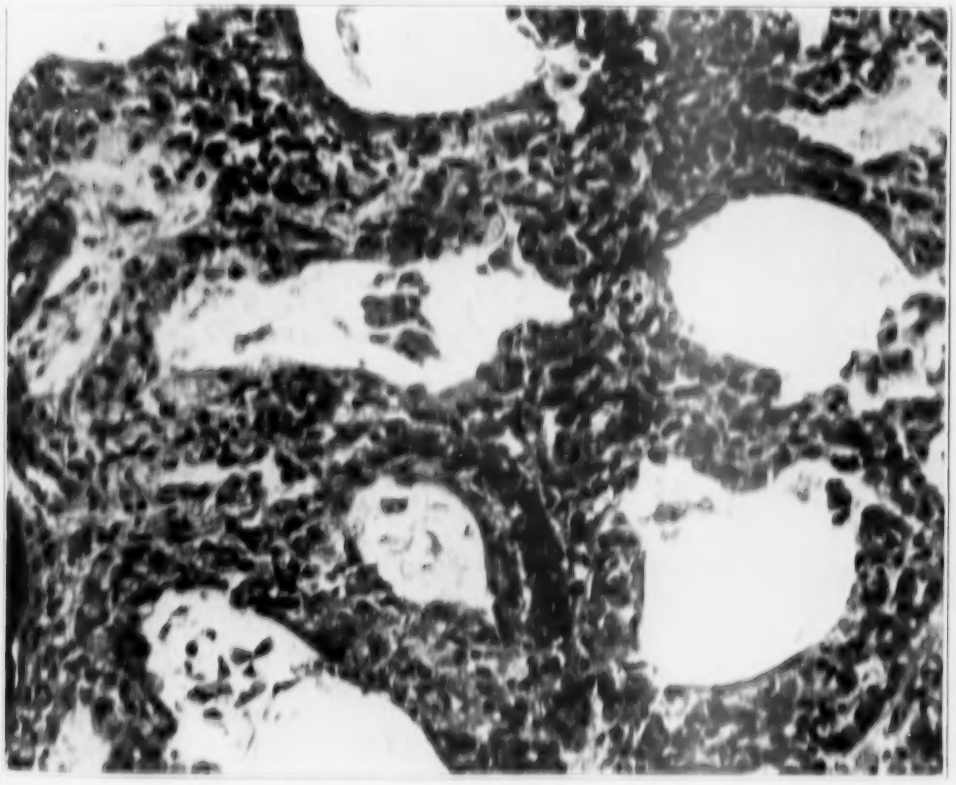

Fig. 8 (case 5).—Multinucleated cell formed from desquamated alveolar epithelium in pneumonia alba. Note the thick alveolar walls and small alveoli; × 250.

cium, 9.9; blood phosphorus, 4.9; urinalysis, albumin and granular casts during last month. Despite vigorous treatment with infusions of dextrose, blood transfusions, doses of neoarsphenamine, mercury and viosterol and ultraviolet irradiation, progress was unsatisfactory and death occurred three months after admission. The clinical diagnosis was: prematurity; congenital syphilis.

Autopsy, performed three and one-half hours after death by Dr. R. A. Moore, revealed: pneumonia alba; syphilitic epiphysitis of the costochondral junctions; acute nephrosis with calcification; renal calculi, right; fatty metamorphosis of the liver, and cloudy swelling of the parenchymatous viscera.

The lungs were large, pale and firm. The pleura was normal. The lung substance cut with increased resistance. The interlobular septums were more distinct than normal and retracted below the lung tissue. Along the anterior margin the alveoli were large and distinct, but within the lung the alveolar markings were obscured. Microscopically, the alveolar walls were thickened by an increase of loose, collagen-poor, fibrous tissue infiltrated with lymphocytes, plasma cells and large mononuclears. The alveoli were inconspicuous and small. The alveolar epithelium was in large part desquamated, and in many areas (fig. 8) the desquamated cells had fused into irregular multinucleated cells. The bronchi and blood vessels were normal. The peribronchial lymph nodes were slightly hyperplastic.

This case is clearly one of syphilitic disease of the lung. At this time the interest in it is limited to the indisputable histologic evidence of the formation of multinucleated cells from desquamated alveolar epithelium. The other evidences of proliferative and exudative inflammation definitely separate it from desquamative pneumonia. It is also evident that the giant cells have no diagnostic relation to syphilis since pneumonia alba may occur without desquamation.

COMMENT

From these five cases it is apparent that large multinucleated cells of variable structure may be found in the lungs of children in a variety of pathologic conditions. Our studies indicate at least four types of cells: (1) the typical Langhans giant cell, (2) the pseudogiant cell formed from fusion of inflammatory exudate, (3) the giant cell derived from bronchiolar epithelium and (4) the multinucleated pulmonary phagocyte.

The Langhans giant cell is from 20 to 40 microns in diameter, with strongly acidophilic cytoplasm and from six to ten small highly chromatic nuclei arranged throughout all portions of the cell but tending to a peripheral position (fig. 1). Mitotic figures have not been observed, and the cytoplasm is free from pigment or other phagocytosed material. This cell is found constantly in the alveoli and never in the connective tissue or bronchi. It is the type described by Hecht [2] and Karsner and Meyers [5] and is probably identical with the giant cells observed by Wood [9] in chemical pneumonia and by MacCallum [6] in postmeasles interstitial pneumonia of adults. With the permission of Dr. Allen Graham and Dr. B. S. Kline we studied two cases of pneumonia, which followed the inhalation of nitric oxide, and observed the same cell type. In serial section, this cell is roughly spherical and does not occur in syncytial masses. Its origin is in doubt, but we believe that it may be formed by fusion of pulmonary phagocytic cells and subsequent degenerative changes, or by a fusion and hyalinization of alveolar exudate.

9. Wood, F. C.: Poisoning by Nitric Oxid Fumes, Arch. Int. Med. **10**:478 (Nov.) 1912.

Borst [7] and Galdi [10] favored a diagnosis of tuberculosis when the Langhans type of cell is present, but Kromayer,[11] Hecht [2] and Ribbert [12] opposed such a view. There is no histologic or bacteriologic evidence of tuberculosis in the case reported here. The association of the typical giant cells with postmeasles pneumonia is striking. Of twenty-seven cases reported by Hecht,[2] nineteen were cases of pneumonia which complicated measles. The case reported by Karsner and Meyers [5] followed measles. In the present case there was no history of previous infectious disease, but there were bands of hyalinized homogeneous or fibrillar material lining many air sacs (fig. 2), which has been described as typical of postinfectious pneumonia, especially influenzal, by Lucké, Wight and Kime.[13] Kromayer's [11] conclusion that giant cells are a constant part of all advanced lobular pneumonia is untenable, since many cases without giant cells are observed. Langhans' giant cells are frequently associated with a subacute peribronchiolitis with slight to moderate obliteration of the bronchiolar lumina, but the giant cells are never found directly in the peribronchial inflammatory tissue.

Firket [14] described Langhans' giant cells in the lung of a goat suffering from subacute pneumonitis. Friedländer [4] observed similar cells in the lungs of rabbits subsequent to section of the recurrent laryngeal nerve, while Lähr [15] induced giant cell formation by the intratracheal insufflation of staphylococci. Hecht [2] failed to produce giant cells after the intratracheal introduction of bacteria, but found abundant multinucleated cells following similar use of metallic salts, ammonia water and tenacious albuminous materials.

From the evidence at hand, the conclusion is that typical Langhans' giant cells may be formed in any subacute or chronic inflammation of the lung when there is delayed resolution associated with a rich fibrinous exudate and an inadequate emptying of the bronchi and bronchioles by cough. Such a hypothesis offers an explanation for the occurrence in postinfectious pneumonia, the higher frequency in children and the

10. Galdi, F.: Ueber eininge von den gewöhnlichen abweichende Pneumonie Formen, Deutsches Arch. f. klin. Med. **75**:239, 1903.

11. Kromayer, E.: Ueber die sogenannte Katarrhal-Pneumonie nach Masern und Keuchbusten, Arch. f. path. Anat. **117**:452, 1889.

12. Ribbert, H.: Die Respirationsorgane, in Brüning and Schwalbe: Handbuch der allgemeinen Pathologie und der pathologischen Anatomie des Kindesalters, Munich, J. F. Bergmann, 1913, vol. 2, p. 465.

13. Lucke, B.; Wight, T., and Kime, E.: Pathologic Anatomy and Bacteriology of Influenza, Arch. Int. Med. **24**:154 (Aug.) 1919.

14. Firket: Pneumonie à cellules géantes chez une chevre d'Afrique, Arch. f. Schiffs- u. Tropen-Hyg. **16**:46, 1912.

15. Lähr, quoted by Hecht, V.: Beitr. z. path. Anat. u. z. allg. Path. **48**:263, 1910.

association with subacute or chronic changes. There is insufficient evidence that such cases should be classified as a distinct type of pneumonia.

The second type of multinucleated cell observed is shown in figure 2. It is of variable size with irregular borders, coarsely granular acidophilic cytoplasm and from three to ten small, highly chromatic, presumably pyknotic nuclei. Such masses are invariably associated with fibrinous masses (fig. 4), and there is little doubt that they are formed by fusion of hyalinized exudate and do not represent true cells. Such masses, composed of degenerated red cells, leukocytes, lymphocytes, strands of fibrin and desquamated epithelial cells, form large sheets occupying many alveoli and connected through the interalveolar pores and infundibuli. They are always confined to the alveolar and infundibular spaces and may or may not be attached to the alveolar wall. This type of multinucleated protoplasmic mass is similar to those observed by Karsner and Meyers.[5] They expressed the belief that it is directly related to the typical Langhans giant cell, but we have been unable to establish definitely histologic evidence of transition.

In a few cases giant cells apparently formed from desquamated bronchial epithelium have been observed (fig. 3). No difficulty is experienced in tracing all transitions from bronchial epithelium to the fully formed multinucleated cell.

Finally, there is the fourth type of cell shown in figure 8. It varies from 15 to 40 microns in diameter, has a nongranular neutrophilic or slightly basophilic cytoplasm and contains from two to six lightly stained vesicular nuclei, from 4 to 6 mm. in diameter, arranged throughout the cell. There are occasional vacuoles in the cytoplasm. They are found in the lung about areas of pneumonia, in one lung or lobe when the other lung or lobes are involved in pneumonia, in association with the exudate in the early and late stages of bronchopneumonia and in extensive desquamation and hyperemia not associated with other histologic signs of inflammation (fig. 6). Such cells frequently contain a large amount of brown, granular, iron-bearing pigment (fig. 5). The presence of this pigment does not prove the presence of a phagocytic function of the multinucleated cells, since the phagocytosis may have occurred previous to fusion. Generally, the multinucleated cells are found within the alveolar spaces, although occasional mononucleated cells of similar morphology are present in the alveolar walls. Despite the latter observation, the bulk of histologic evidence indicates that they are formed from desquamated alveolar epithelium.

Our observations indicate that desquamation and giant cell formation can occur independently of alveolar exudation and represent a distinct type of reaction, termed by the French school as "alveolite" and the German school as "pneumonic desquamativ." The formation is asso-

ciated with slight infiltration of the alveolar walls with lymphocytes and an occasional polymorphonuclear leukocyte. Despite the small amount of exudation in the alveolar walls, the essential nature of the process is a swelling and desquamation of the alveolar epithelium, and it should be classified as an alterative inflammation.

The same processes, to a more marked degree, are observed in the desquamative type of pneumonia alba, but in this case the desquamation and giant cell formation are associated with a proliferative and exudative inflammation.

CONCLUSIONS

1. At least four types of multinucleated cells are found in inflammations of the lung in children.

2. Multinucleated cells may be formed by fusion of degenerated exudate, desquamated bronchial epithelium and desquamated alveolar epithelium.

3. There is no evidence that pneumonia associated with multinucleated cells constitutes a distinct type.

4. Extensive desquamation and giant cell formation may occur independent of alveolar exudation, and may be either a distinct type of alterative inflammation of the lung or a part of the pathologic changes of pneumonia alba.

5. Giant cells in association with pneumonia have no specific cause.

BUFFER CAPACITIES OF VARIOUS MILKS AND PROPRIETARY INFANT FOODS*

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The rôle of acidity in digestion depends on the H-ion concentration rather than on the titratable acidity. In experiments with normal breast-fed infants, Marriott and Davidson [1] came to the conclusion that optimum gastric acidity was reached one and one-half hours after feeding and was maintained for one hour. The range of H-ion concentration during the period of optimum gastric digestion was found to be from p_H 3.5 to 5, the average being p_H 3.75.

With an increase in the age of infants there is a gradual increase in the H-ion concentration, while disease, malnutrition and infections generally lower the H-ion concentration attained in the stomach.

Cow's milk has a relatively great buffer capacity over the range of H-ion concentration concerned in digestion, and therefore requires a relatively high gastric secretion as compared with that necessary when infants are breast fed.[1]

Attempts have been made to modify cow's milk so that it will conform more closely in various properties to human milk. Many of these modifications have been in sugar and fat contents and in their constituents and hence will not be considered here since they are not directly concerned in reactions involving the ions of acidity. Modifications involving changes in ash or acid content, however, are important from the standpoint of buffer values.

Although buttermilk has long been used as an infant food in cases of digestive disturbances, Klotz [2] was perhaps the first to administer to infants milk to which acid had been added.

In 1919, Marriott and Davidson [3] called attention to the lessened gastric secretion of sick infants and advised the use of acidified milk, especially in the case of athreptic infants.

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* Submitted for publication, Feb. 13, 1930.

* From the Research Laboratory, Bureau of Dairy Industry, U. S. D. A., Washington, D. C.

1. Marriott, McK., and Davidson, L. T.: The Acidity of the Gastric Contents of Infants, Am. J. Dis. Child. **26**: 542 (Dec.) 1923.

2. Klotz, M.: Milchsaüre und Säuglingsstoffwechsel, Jahrb. f. Kinderh. **70**: 1, 1909.

3. Marriott, McK., and Davidson, L. T.: The Artificial Feeding of Athreptic Infants, J. A. M. A. **73**: 1173 (Oct. 18) 1919.

Acidification of cow's milk makes possible the feeding of larger and more concentrated rations without increasing correspondingly the gastric secretion of acid.

Later, the same authors [4] advocated the use of acidified whole cow's milk as a routine infant food, stating "that the supposition that infants are incapable of digesting milk of 3.50 per cent protein content under these conditions is based on an assumption unsupported by experimental evidence."

Any modification of cow's milk involving changes in the percentage composition of the constituents other than fat and lactose affects the

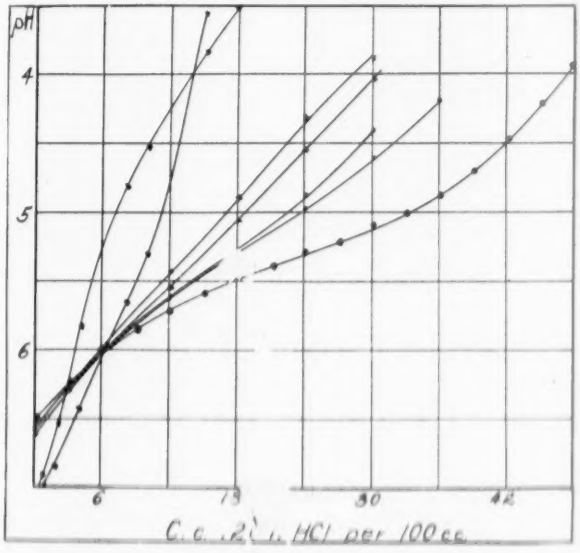

Chart 1.—Titration curves on milks from different species. The dotted line (the lowest line) indicates the curve on goat's milk; the triangle lines (the upper two lines), the curve on breast milks, and the crossed and the small dot lines, the curve on cow's milk.

ease with which its H-ion concentration is changed in the infant stomach, or its buffer value, and is therefore of particular interest in this respect.

In the following detailed experiments, an attempt has been made to evaluate quantitatively the buffer intensities of various milks and infant foods over the range of H-ion concentration concerned in digestion.

4. Marriott, McK., and Davidson, L. T.: Acidified Whole Milk as a Routine Infant Food, J. A. M. A. 81:2007 (Dec. 15) 1923.

EXPERIMENTAL WORK

Human, Cow's and Goat's Milk.—These milks or their modifications have always served as infant foods, although they differ widely in the relative proportions of their constituents, as indicated in table 1.

With respect to acid-base relationships and curd formations, their ash and albumin contents respectively are of interest. The former is related directly to the buffer action as indicated in the following data, while the albumin content greatly influences the type of curd formed and will be discussed later.

The following curves were plotted from the titration data on one sample of goat's milk; four samples of cow's milk differing in their solids-not-fat content, and two samples of breast milk drawn at different periods following parturition.

TABLE 1.—*Average Composition of Human, Cow's and Goat's Milk*

Species	Water, per Cent	Casein, per Cent	Albumin, per Cent	Fat, per Cent	Lactose, per Cent	Ash, per Cent
Human	87.41	0.91	1.23	3.76	6.29	0.31
Cow	87.27	2.95	0.52	3.66	4.91	0.69
Goat	84.14	3.04	0.99	6.00	5.02	0.81

The data indicate considerable difference in these milks in the amounts of added acid that is necessary to produce a H-ion concentration represented by p_H 5.

Comparative values for their buffer intensities at the various ranges of H-ion concentration may be obtained by calculating the buffer index, $\frac{dB}{dp_H}$ for each small increment of added acid, as follows:

$$\frac{dB}{dp_H} = \frac{\text{cc. acid added to produce } p_H \text{ change} \times \text{Normality factor of acid}}{\text{Av. dilution at av. } p_H \text{ range} \times \text{Change in } p_H \text{ units}}$$

If 6 and 12 cc. of two-tenths normal acid were added respectively to two samples of 100 cc. of a milk and the observed difference in their H-ion concentrations in p_H units were 0.4, the substituted values would be as follows:

$$\frac{(12 - 6) \times 0.2}{100 + \frac{12 + 6}{2} \times 0.4}$$

The value $\frac{dB}{dp_H}$ represents, therefore, the equivalents of acid (or base) necessary to change the H-ion concentration the equivalent of one p_H unit, and is assigned to the midpoint of each p_H range involved.

The buffer intensities calculated in this manner, from the values shown in chart 1, are plotted in chart 2.

These results indicate that practically the entire acid buffering in milks occurs in the range of from p_H 5 to 6.[5] The buffer intensities are indicated by the plotted values, while the buffer capacities are indicated by the areas prescribed by each curve.

Proprietary Infant Foods.—As heretofore stated, the modifications of milks affecting their percentage composition of carbohydrates and fats change their buffer capacities but slightly. Furthermore, the formulae for reconstitution are usually based to a large extent on their protein contents, which generally bear direct relationship to the ash

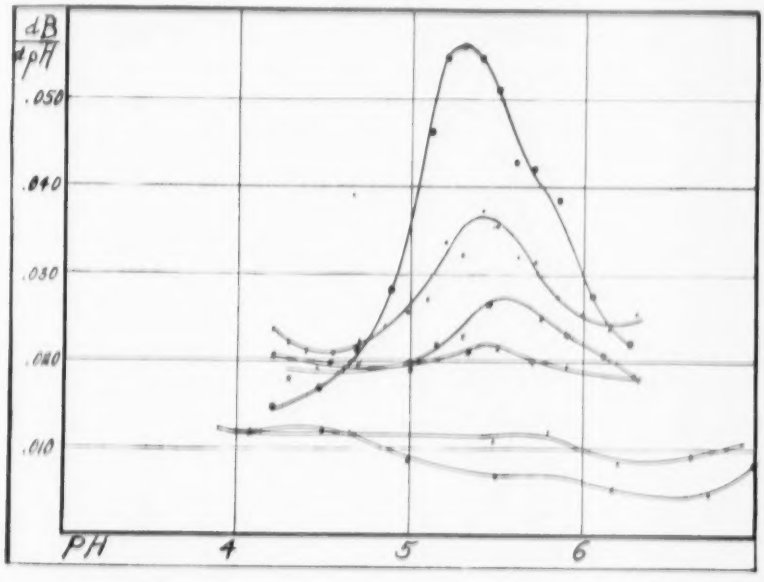

Chart 2.—Buffer intensity curves of milks from different species. The dotted line (the uppermost line) indicates the curve on goat's milk; the crossed lines (the next three), the curve on cow's milk and the triangle lines (the two lowest lines), the curve on breast milk.

contents. As may be expected, therefore, the buffer capacities per unit weight of milk solids-not-fat should be quite comparable.

Statements are frequently made by manufacturers, however, that their compositions have been so modified that the product more nearly resembles breast milk. In the light of the work of Marriott and his co-workers,[6] and of Brennemann,[7] it seems that the behavior of a

5. Whittier, E. O.: Buffer Intensities of Milk and Milk Constituents: I. Buffer Action of Casein in Milk, J. Biol. Chem. **83**:79, 1929.

6. Marriott and Davidson (footnotes 3 and 4).

7. Brennemann, J.: The Coagulation of Cow's Milk in the Human Stomach, Arch. Pediat. **34**:81, 1917.

product in the infant's stomach may be of greater importance than is its resemblance to breast milk in percentage composition.

Five samples of proprietary infant foods were procured and reconstituted as directed on the labels of their containers. Table 2 indicates the composition of these reconstituted products and also the composition of a breast milk and of a cow's milk diluted 1 : 1 to make it comparable with the other milks in protein and salt content.

Similar to the procedure with the milks already discussed, the products were titrated with two-tenths normal hydrochloric acid. The results are shown in chart 3, in which is also included the titration data on an undiluted lactic acid milk.

The parallel relationship between the titration curves of the proprietary infant foods (excepting nos. 3 and 7) and that of diluted milk indicates no great modification which affects acid-base relationships.

TABLE 2.—*Composition of Human Milk, Reconstituted Infant Foods and Diluted Cow's Milk*

	Cow's Milk Dil. 1:1, per Cent	Proprietary Infant Foods, per Cent					Human Milk, per Cent
	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5	Sample 6	Sample 8
Protein	1.70	1.3-1.4	1.3-1.4	2.03	1.54	1.70	2.14
Ash or salts	0.37	0.25-0.30	0.25-0.30	0.44	0.40	0.32	0.21
Carbohydrate	2.46	7.3-7.5	7.3-7.5	6.66	6.80	7.10	6.29
Fat	1.80	3.5-3.6	3.5-3.6	3.12	3.40	4.06	3.76

Chart 4 illustrates the buffer intensities of each milk in various regions of H-ion concentration. Of these, only breast milk and the product no. 3 exhibit buffer intensities of less magnitude than those of diluted cow's milk over the range of H-ion concentration shown.

The average intensity for each sample between its initial H-ion concentration and that signified by a p_H of approximately 4 was also calculated and is given in table 3.

These figures may be considered as the relative values of their buffer capacities over the range of H-ion concentration given and indicate that within the approximate range of H-ion concentration concerned in the stomach the proprietary infant foods nos. 2 and 6 differ little from average diluted cow's milk in their buffer capacities. Samples nos. 4 and 5 have buffer capacities greater than that of diluted cow's milk, and only no. 3 approaches breast milk in this respect.

Lactic acid milk, although it has an initially high H-ion concentration, has also a great buffer capacity and requires relatively large amounts of acid to vary its H-ion concentration one p_H unit. However, since its initial H-ion concentration is high, its buffer capacity would have little significance. In the region of H-ion concentration represented by p_H 3 to 4 the normal buffer action of the acids added must be

considered. In this region and in regions of greater H-ion concentration, the buffer index is not entirely a measure of the buffer intensity of the product in solution but also that of the normal buffering capacity of the acid added.[5]

Heated Milks.—The statement has been made by Marriott [8] that evaporated milk possesses an advantage over other milks for the preparation of lactic acid milk in that it possesses a slightly lower buffer value than does ordinary cow's milk because of the fact that part of the

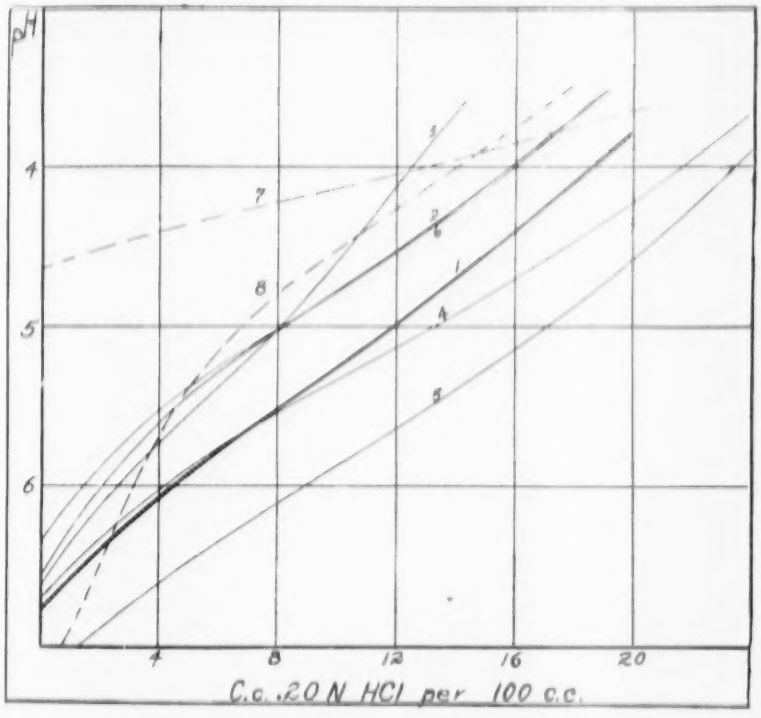

Chart 3.—Titration curves on various reconstituted infant foods, diluted cow's milk, breast milk and an acidified cow's milk. Line 1 indicates the cow's milk (dil. 1:1); lines 2, 3, 4, 5 and 6, the proprietary infant foods; line 7, the lactic acid milk and line 8, the breast milk.

TABLE 3.—*Average Buffer Intensities of Various Milks Over pH Range—Approximately 4 to Initial pH*

Cow's Milk Dil. 1:1, per Cent	Proprietary Infant Foods, per Cent					Human Milk, per Cent
Sample 1	Sample 2	Sample 3	Sample 4	Sample 5	Sample 6	Sample 8
0.0122	0.0124	0.0080	0.0146	0.0184	0.0115	0.0084

8. Marriott, McK.: Preparation of Lactic Acid Milk Mixtures for Infant Feeding, J. A. M. A. **89**:862 (Sept. 10) 1927.

calcium and phosphates have been converted into insoluble calcium phosphates in the sterilization process. In the regions of higher H-ion concentrations concerned here the calcium phosphates are soluble, and therefore, although the regions of greatest buffer intensity with respect to H-ion concentration may be shifted, the buffer capacities will vary but slightly. Chart 5 illustrates the buffer intensities of two normal unsterilized milks, *A* and *B*, and the reconstituted evaporated and sterilized products *A*'s and *B*'s.

Although sterilization has caused a shifting of the regions of maximum buffer intensity, the average buffer intensities, or their buffer capacities, as indicated by the areas prescribed by the respective curves

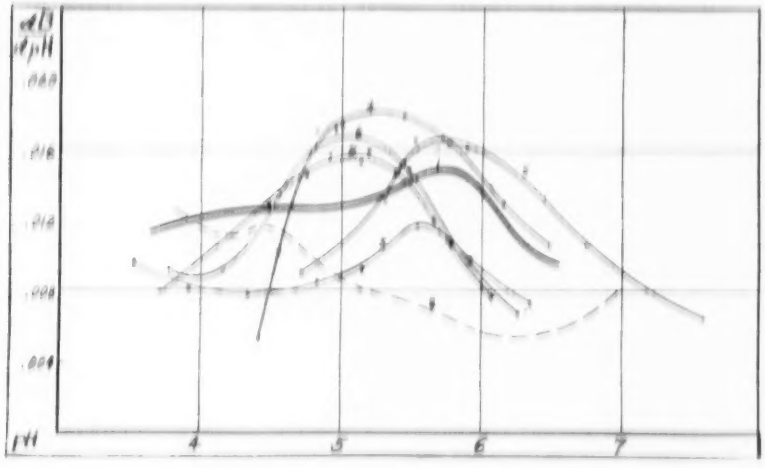

Chart 4.—Buffer intensity curves on milks, the titration data of which are shown in chart 3.

in each case, are approximately of the same magnitude. This may be verified by calculations of the average buffer intensities.

Curd Formation.—Raw cow's milk coagulates in the human stomach within a few minutes, forming large and relatively tough curds. The curds formed from pasteurized milk are somewhat softer while those from boiled milk are small and soft. With dilution of the milk there is a decrease in the size of the curds formed and in their compactness.[7]

The latter fact is of interest with respect to goat's milk, which has a milk solids-not-fat concentration greater than that of cow's milk and still forms a fine curd on coagulation. Goat's milk also has a relatively great buffer capacity and still is tolerated well by some infants. Its favorable action is undoubtedly due to the finely divided coagulum which forms when it is acidified.

The formation of a finely divided curd is undoubtedly due to a large extent in this case, to a high percentage of albumin content and illustrates the general effect of colloidal protective agents, such as those present in barley water.

The protective action of barley is due largely to the extracted starch and a small amount of proteins. The extract contains also some of the salts of the grain, the amounts being so small that the added buffer capacity resulting from its uses is negligible.

Other starchy materials such as flours have also been used to a limited extent in the preparation of infant foods. They exert a protective action in coagulation and add relatively little to the buffer capacity

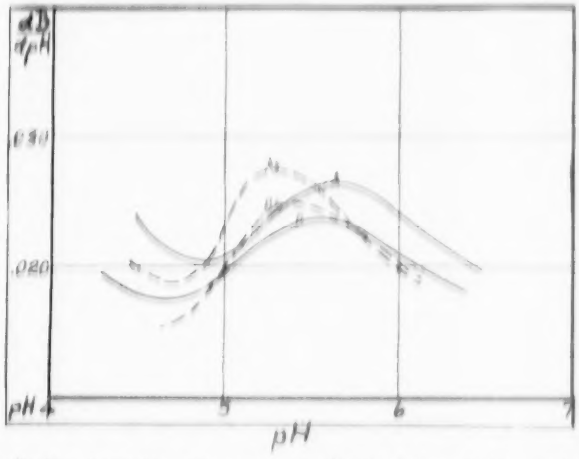

Chart 5.—Buffer intensity curves on sterilized (*A*s and *B*s) and unsterilized (*A* and *B*) samples of two milks.

since the average buffer intensity of 20 per cent patent flour suspension over a range of H-ion concentration of from p_H 5 to 7 is approximately 0.0021,[9] a relatively low value when compared with that of normal milk.

Acid coagulation tests were made on the milks on which the data in table 2 were obtained. The proprietary preparations (except no. 3) differed slightly from cow's milk with respect to the type of the curd formed. Milk no. 2 formed a fluffier curd than did any of the other samples with the exception of breast milk.

Although there is a general correlation between buffer capacities and types of curd formed in these cases, it is probably accidental. Other experiments not discussed here indicate that the correlation is not neces-

9. Holm, G. E., and Grewe, E.: The Buffer Intensities of Water Extracts and Suspensions of Various Flours at Different H-Ion Concentrations, Cereal Chem. 7:49, 1930.

sarily a direct one. The preceding as well as the following discussion also indicates that there may be no direct correlation between buffer capacity and type of curd formed.

Precoagulated milks show little tendency to recoagulate into a mass. The favorable action of buttermilk and other acid milks and also of evaporated milks may therefore be attributed to a large extent to this property rather than to buffer capacity variations. In the case of dried milks wherein fine curds result on coagulation with acids, the explanation lies probably in the effect of denaturization of the proteins on their structure-forming properties when coagulated.

In view of these facts, it seems probable that in the majority of cases of infant feeding the nature of the curds formed is of greater importance than is the buffer capacity.

THE INSENSIBLE PERSPIRATION IN INFANCY AND IN CHILDHOOD

III. BASAL METABOLISM AND BASAL INSENSIBLE PERSPIRATION OF THE NORMAL INFANT: A STATISTICAL STUDY OF RELIABILITY AND OF CORRELATION *

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AND
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NEW YORK

In a recent communication [1] tentative standards were proposed for the basal insensible perspiration of normal infants analogous to the well known standards at present available for their basal metabolism. Before accepting the newly proposed standards, it seemed advisable to make a comparative study of the reliability of the two series of basal standards. Such a study would also serve to show any correlation that might exist between the two physiologic mechanisms. If the correlation were shown to be of high degree, the data might afford a possible method of predicting the probable metabolism of infants from their measured insensible perspiration. This procedure would be especially valuable since present methods of estimating the respiratory exchange of infants are time-consuming and technically difficult compared with the relatively simple method of weighing for measuring their insensible loss.[2] Since evidence of reliability and of correlation in both instances involved the employment of statistical methods, it seemed feasible to report the results of both studies in this communication.

PLAN OF STUDY

An evaluation of the validity of basal standards for metabolism and insensible perspiration of normal infants seemed best achieved by a statistical analysis of the original data from which the standards were

* Submitted for publication, Feb. 21, 1930.

* From the Department of Pediatrics, Cornell University Medical College and the New York Nursery and Child's Hospital.

* This investigation was supported in part by the Committee for the Encouragement of Medical Research.

1. Levine, S. Z.; Kelly, M., and Wilson, J. R.: The Insensible Perspiration in Infancy and in Childhood: II. Proposed Basal Standards for Infants, Am. J. Dis. Child. **39**:917 (May) 1930.

2. Levine, S. Z.; Wilson, J. R., and Kelly, M.: The Insensible Perspiration in Infancy and in Childhood: I. Its Constancy in Infants Under Standard Conditions and the Effect of Various Physiologic Factors, Am. J. Dis. Child. **37**:791 (April) 1929.

derived. The published data of Benedict and Talbot [3] and of Levine, Kelly and Wilson [4] for heat production and insensible perspiration, respectively, were considered adequate for such treatment, since they included large numbers of normal infants of similar age, and since the two series of measurements were invariably made under strictly comparable (basal) conditions. Because of the homogeneous character of the material, it was also utilized as part of the following study of correlation between the two variables.

Evidence of correlation between metabolism and insensible perspiration in the human subject and particularly in the infant was derived from data collected from a number of sources.[4] These data included published material secured in simultaneous calorimetric measurements [5] and also material obtained in independent measurements with the respiration chamber and balance, respectively.[6] A statistical analysis of this material was undertaken as an index of the causal relationship present in the human subject between the two variables.

In addition, this statistical evidence of correlation was controlled experimentally by actual measurements of the insensible perspiration of a group of infants with the balance and of the metabolism of the same subjects with the respiration chamber under comparable conditions. A slight modification of the latter method was successfully used in the study of adults by Benedict and Root,[7] but its application to infants is technically difficult and subject to several sources of error. Only a limited number of infants, therefore, were studied in this manner. The data which were reported in a preliminary paper [8] will be incorporated later in this communication.

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3. Benedict, F. G., and Talbot, F. B.: Metabolism and Growth from Birth to Puberty, Carnegie Institution of Washington, Pub. 302, 1921, tables 27 and 28.

4. Levine, Kelly and Wilson (footnote 1). Benedict and Talbot (footnote 3). Soderstrom, G. F., and Du Bois, E. F.: Water Elimination Through Skin and Respiratory Passages in Health and Disease, Arch. Int. Med. **19**:931 (May) 1917. Levine, S. Z., and Wilson, J. R.: The Respiratory Metabolism in Infancy and in Childhood: IV. Elimination of Water Through the Skin and Respiratory Passages of Children, Am. J. Dis. Child. **33**:204 (Feb.) 1927; The Respiratory Metabolism in Infancy and in Childhood: VII. Elimination of Water Through the Skin and Respiratory Passages of Infants, ibid. **35**:54 (Jan.) 1928. Levine, S. Z.; Wilson, J. R., and Kelly, M.: Prediction of the Basal Metabolism of Infants from Their Measured Insensible Perspiration, Proc. Soc. Exper. Biol. & Med. **25**:554, 1928.

5. Soderstrom and Du Bois (footnote 4, third reference). Levine and Wilson (footnote 4, fourth and fifth references).

6. Levine, Kelly and Wilson (footnote 1). Benedict and Talbot (footnote 3).

7. Benedict, F. G., and Root, H. F.: Insensible Perspiration: Its Relation to Human Physiology and Pathology, Arch. Int. Med. **38**:1 (July) 1926.

8. Levine, S. Z.; Wilson, J. R., and Kelly, M.: Prediction of the Basal Metabolism of Infants from Their Measured Insensible Perspiration, Proc. Soc. Exper. Biol. & Med. **25**:554, 1928.

The apparatus, technic of measurements, experimental conditions, sources of error and detailed data of the respective observations for heat production and insensible perspiration were fully considered in the original papers.[9]

RESULTS

The results will be presented under the three following headings: (1) reliability of available standards for basal metabolism and basal insensible perspiration of normal infants; (2) magnitude of correlation between the two variables (*a*) in simultaneous measurements and (*b*) in independent measurements, and (3) prediction of probable metabolism of infants from their measured insensible perspiration. The evidence, statistical and experimental, which bears on the reliability of the proposed method of prediction is reviewed.

Validity of Basal Standards.—The original data of Levine, Kelly and Wilson [1] and of Benedict and Talbot [3] were subjected to statistical treatment. They comprised 91 basal observations of the insensible loss of eighty-five normal infants covering the period from birth to 25 months of age [1] and 130 basal metabolic determinations on a comparable group of infants.[3] This material both in point of numbers and in accuracy may be considered adequate for such treatment. The statistical methods employed will be fully described subsequently (table 2). All calculations presented in this communication were made by one and checked by a second observer.

From the original data, coefficients of correlation were calculated both for basal metabolism and for basal insensible perspiration referred to age, weight, height and surface area. These constants for each of the eight pairs of variables with their respective probable errors are shown in table 1.

The coefficient of correlation is generally accepted in statistical work as indicating the magnitude of causal relationship between two variables. All of the coefficients shown in table 1 are of a high order of magnitude. With perfect correlation represented by unity, these high coefficients which exceeded 0.9 in all except one instance (0.8927 for basal metabolism and age) verify by statistical methods the constant relationship long recognized between basal metabolism and the physical factors enumerated in this table. Of greater interest is the demonstration of an equally consistent relationship between basal insensible perspiration and these factors. One notes that the correlation coefficients for insensible loss are consistently of a higher order than those for heat production. Statistical analysis of the differences, however, indicates that they are

9. Levine, Wilson and Kelly (footnotes 1 and 2). Benedict and Talbot (footnote 3). Soderstrom and Du Bois (footnote 4, third reference). Levine and Wilson (footnote 4, fourth and fifth references).

not significant except in the case of surface area. In this instance, the difference of the coefficients exceeds by a significant value the difference of their probable errors, being 0.0313 and 0.0104, respectively.[10] In this connection, it is of interest to point out that the highest correlation coefficient is that between surface area and basal insensible perspiration (0.9573 ± 0.0059). This result is in accord with theoretic expectation, since one of the main channels of insensible loss is by way of evaporation of moisture from the surface of the body. It is also noteworthy that the correlation coefficient between height and basal metabolism is of a higher order than the coefficients for either weight or surface area. This calculation confirms the recent opinion of Benedict and of Talbot [11] that for the age period below puberty basal metabolic standards based on body stature may be more reliable than those referred to either weight or surface area.

TABLE 1.—*Coefficients of Correlation* *

Variables	Number of Observations	Coefficient of Correlation with Probable Error
Surface Area		
Metabolism	125	0.9260 ± 0.0086
Insensible perspiration	91	0.9573 ± 0.0059
Weight		
Metabolism	121	0.9275 ± 0.0086
Insensible perspiration	91	0.9510 ± 0.0068
Height		
Metabolism	134	0.9435 ± 0.0065
Insensible perspiration	88	0.9458 ± 0.0077
Age		
Metabolism	138	0.8927 ± 0.0117
Insensible perspiration	91	0.9091 ± 0.0121

* The subjects included in the two series (metabolism and insensible perspiration) invariably fell within the same range of physical measurements; namely, from birth to 25 months of age, from 2.5 to 11.6 Kg. in weight, from 47 to 85 cm. in height and from 0.175 to 0.450 sq. m. in surface area.

The results verify by statistical methods the reliability of the tentative standards for the basal insensible perspiration of normal infants based on age, weight, height and surface area, respectively, which were proposed in the preceding paper of this series,[1] and indicate that they compare favorably in reliability with the generally accepted standards for the basal metabolism of these subjects referred to the same factors.

Correlation Between Metabolism and Insensible Perspiration in Simultaneous Measurements.—Evidence of intrinsic correlation between the two mechanisms is not lacking. Calorimetric studies [6] have shown that under standard conditions of clothing, temperature and humidity, the human subject loses a constant proportion of approximately 25 per

10. The difference of the probable errors equals the square root of the sum of the squared individual errors.

11. Benedict, F. G.: Physical Factors in Predicting the Basal Metabolism of Girls, Proc. Am. Philos. Soc. **63**:25, 1924. Talbot, F. B.: Basal Metabolism in Children, Physiol. Rev. **5**:477 (Oct.) 1925.

cent of his total heat in vaporization of water through skin and respiratory passages. This relationship between heat production and heat loss in vaporization was maintained from infancy to old age and in all of the afebrile diseases investigated.

A priori, a corresponding relationship should be demonstrable between metabolism and insensible perspiration, since the chief constituent of the latter is water vapor.[12] With this expectancy in mind, the

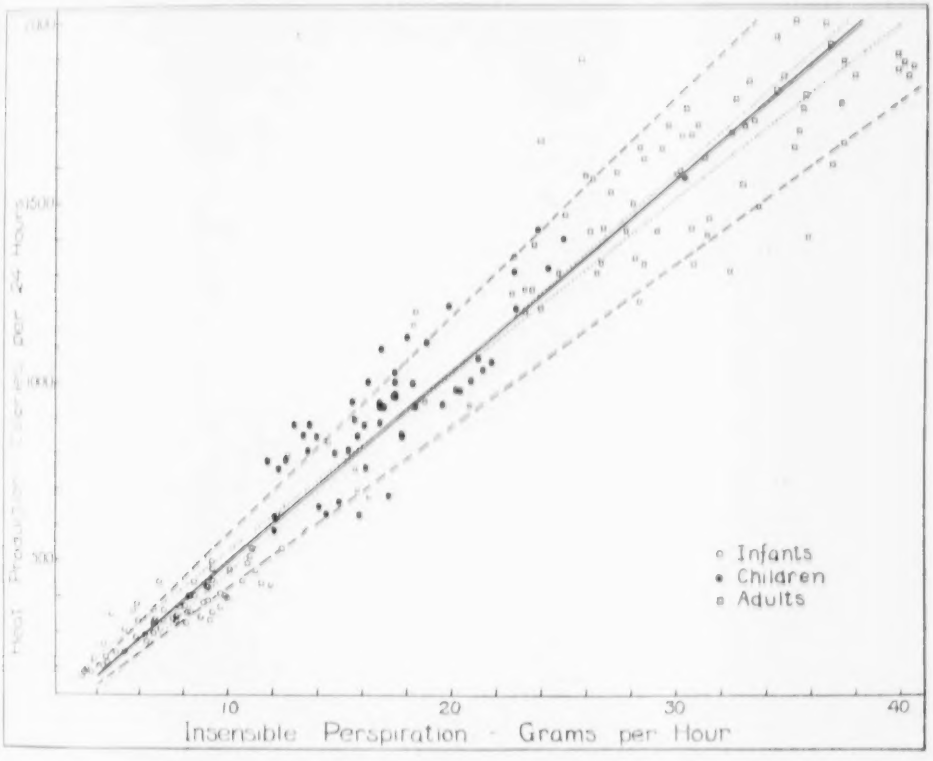

Chart 1.—Relationship in simultaneous measurements of metabolism to insensible perspiration from infancy to old age. The broken lines indicate a deviation of 15 per cent from the smoothed curve as laid out. The dotted lines represent the regression lines computed by statistical methods.

calorimetric data already cited were analyzed, and the results are graphically presented in chart 1. The data on adults were secured with the

12. The insensible loss includes all of the invisible gaseous emanations which leave the body by way of the skin and respiratory passages. As measured by the method of weighing, its chief component is water vapor (excluding visible perspiration), but it also contains exhaled carbon dioxide less simultaneously absorbed oxygen and traces of other gases. Under ordinary conditions, moisture constitutes from 85 to 90 per cent of the total insensible loss.

Russell-Sage calorimeter;[13] those on children and infants, with the respiration chamber at the New York Nursery and Child's Hospital.[14] The number of observations recorded in the chart totals 196. Each point represents a simultaneous measurement of heat production in calories per twenty-four hours and of insensible perspiration in grams per hour. The latter was calculated from the carbon dioxide exhaled, the oxygen consumed and the water vaporized by subjects during observations.

The correlation between heat production and insensible perspiration in simultaneous measurements is striking. A smoothed curve constructed according to standard statistical methods takes the form of a straight line.[15] From infancy to old age, the formation within the body of approximately 50 calories of heat per twenty-four hours (2 calories per hour) is accompanied under standard conditions by a loss in weight of 1 Gm. per hour through the medium of insensible perspiration. Relatively few of the points deviate from the curve as laid out by more than ± 15 per cent. The scatter is remarkably good when one considers the many errors inherent in measurements of moisture by the chamber method.

The original data[5] employed in the construction of the smoothed curve in chart 1 were analyzed statistically in order to measure the precise degree of correlation between the two variables.[16] Table 2 is arranged to show the successive steps of a representative analysis. As previously noted, the same procedure was followed in the calculations of the correlation coefficients summarized in table 1.

Statistical treatment of the data establishes the causal relationship between heat production and insensible perspiration in the human subject. The notably high coefficient of correlation of 0.9417 ± 0.0064 between the variables unequivocally eliminates the factor of random sampling. A similar analysis of the sixty-two observations on infants in the series also showed a high correlation coefficient between the characters (0.8885 ± 0.0180).

By the use of formulas shown in table 2, theoretical regression curves for heat production and insensible perspiration were computed for the entire series of observations.[17] The computed curves (in

13. Soderstrom and Du Bois (footnote 4, third reference).

14. Levine and Wilson (footnote 4, fourth and fifth references).

15. All of the observed curves of correlation presented in this paper were smoothed according to statistical methods by plotting lines through averages of the points representing groups of overlapping observations at graduated intervals.

16. Pearl, R.: Medical Biometry and Statistics, Philadelphia, W. B. Saunders Company, 1923, ch. 14.

17. Regression lines afford a graphic method of measuring the magnitude of correlation between two variables (footnote 16).

TABLE 2.—*Correlation of Insensible Perspiration and Metabolism in Simultaneous Measurements*

TABLE 2.—*Correlation of Insensible Perspiration and Metabolism in Simultaneous Measurements*

Metabolism, Calories per 24 Hours	Insensible Perspiration, Gm. per Hour												f Frequency of Metabolism in Class Units	v Metabolism in Class Units of 200 Calories per 24 Hours	fx Times x	fx² Times x²	FXy	yFXy
	0–3.99	4.00–7.99	8.00–11.9	12.0–15.9	16.0–19.9	20.0–23.9	24.0–27.9	28.0–31.9	32.0–35.9	36.0–39.9	40.0–43.9	44.0–47.9						
0– 199	4	—	—	—	—	—	—	—	—	—	—	—	4	−5	−20	100	−20	100
200– 399	1	26	12	—	—	—	—	—	—	—	—	—	39	−4	−156	624	−145	580
400– 599	—	1	17	2	—	—	—	—	—	—	—	—	20	−3	−60	180	−59	177
600– 799	—	—	1	12	3	—	—	—	—	—	—	—	16	−2	−32	64	−30	60
800– 999	—	—	—	11	17	3	—	—	—	—	—	—	31	−1	−31	31	−29	29
1000–1199	—	—	—	—	6	5	—	—	—	—	—	—	11	0	0	0	−6	0
1200–1399	—	—	—	—	1	7	6	5	1	—	—	—	19	+1	+19	19	+16	16
1400–1599	—	—	—	—	—	1	8	8	3	1	—	—	21	+2	+42	84	+37	74
1600–1799	—	—	—	—	—	—	1	9	8	2	—	—	20	+3	+60	180	+51	153
1800–1999	—	—	—	—	—	—	1	—	8	6	3	3	17	+4	+68	272	+70	280
2000–2199	—	—	—	—	—	—	—	—	1	—	—	—	1	+5	+5	25	+3	15
2200–2399	—	—	—	—	—	—	—	—	—	—	1	—	1	+6	+6	36	+5	30
F = frequency of insensible perspiration in class units	5	27	30	25	27	16	16	22	12	9	4	3	200 = n or total frequency		Total fx = −99	Total fx² = 965	Total FXy = −117	Total yFXy = 1524
X = insensible perspiration, class unit 4 Gm. per hour	−5	−4	−3	−2	−1	0	+1	+2	+3	+4	+5	+6						
F times X	−25	−108	−90	−50	−27	0	+16	+44	+36	+36	+20	+18	Total F(X) = −117					
F times $(X)^2$	125	432	270	100	27	0	16	88	108	144	100	108	Total F$(X)^2$ = 1519					

The arbitrary origin of X = 22 Gm. of insensible perspiration per hour.
The arbitrary origin of y = 1,100 calories per 24 hours.
The proportionate moments in class units about these arbitrary origins are:

$$v_{1x} = \frac{-117}{200} = -0.585 \qquad v_{1y} = \frac{-99}{200} = -0.495$$

$$v_{2x} = \frac{1559}{200} = 7.795 \qquad v_{2y} = \frac{1675}{200} = 8.375$$

$$v_{xy} = \text{the cross-product about the arbitrary origin} = \frac{1524}{200} = 7.62$$

The mean of X = arbitrary origin + v_{1x} in actual units = 22.0 + (−0.585) (4) = 19.66

The mean of y = arbitrary origin + v_{1y} in actual units = 1100 + (−0.495) (200) = 1001

The cross-product moment about the means = $u_{xy} = v_{xy} - (v_{1x})(v_{1y}) = 7.62 - (-0.585)(-0.495) = 7.330$

u_{2x} The second moment about the mean = $v_{2x} - (v_{1x})^2 = 7.795 - 0.342 = 7.453$

u_{2y} = the second moment about the mean = $v_{2y} - (v_{1y})^2 = 8.375 - 0.245 = 8.130$

γ = correlation coefficient = $\frac{7.330}{(2.730)\ (2.851)} = 0.9427 \pm 0.0064$

$\sigma_x = \sqrt{u_{2x}} = \sqrt{7.453} = 2.730$ in class units

$\therefore \sigma_x$ in actual units = (2.730) (4) = 10.92

$\sigma_y = \sqrt{u_{2y}} = \sqrt{8.130} = 2.851$ in class units

$\therefore \sigma_y$ in actual units = (2.851) (200) = 570.2

P. E. $\gamma = \frac{0.6745\ (1-\gamma^2)}{\gamma\ 200} = 0.0064$

Formulas for regression lines:

For insensible perspiration: $x - \text{mean}_x = (\gamma_{xy}\frac{\sigma_x}{\sigma_y})(y - \text{mean}_y)$, $x = 0.0098y + 1.61$

For metabolism: $y - \text{mean}_y = (\gamma_{xy}\frac{\sigma_y}{\sigma_x})(x - \text{mean}_x)$, $y = 49.17x + 58.3$

broken lines) closely approximate the observed smoothed curve as laid out in chart 1. This evidence confirms the accuracy of the observed curve as plotted and affords additional statistical proof of the consistent relationship between the two variables in simultaneous measurements.

Correlation in Infants Between Metabolism and Insensible Perspiration in Independent Measurements.—To be of practical value for predicting the metabolism of infants from their measured insensible perspiration, it was first necessary to show that measurements of the insensible loss by means of the balance did not impair the intrinsic

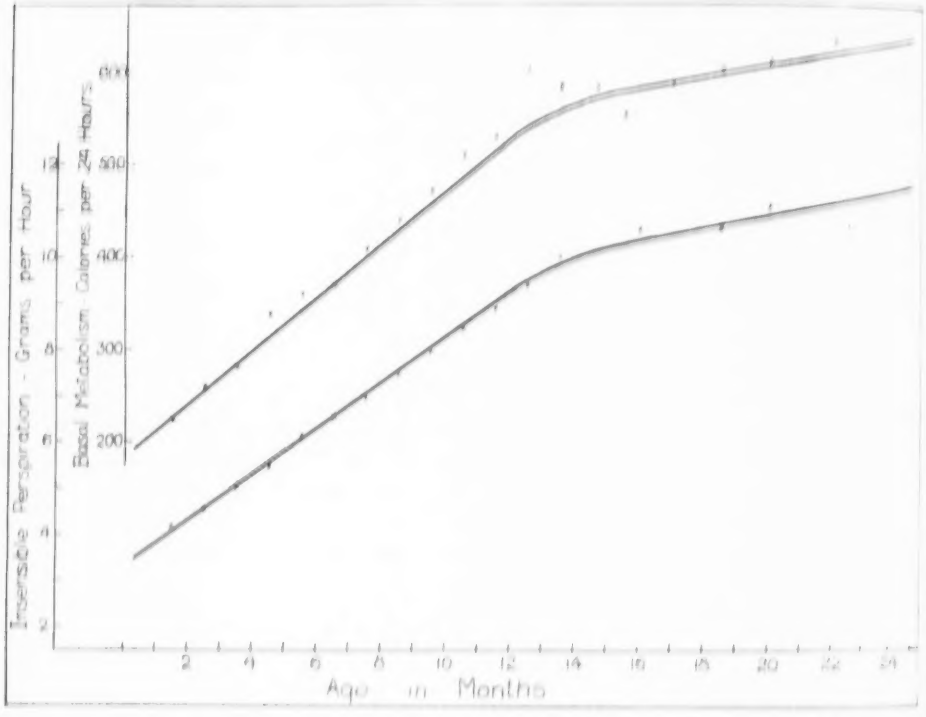

Chart 2.—Relationship in infants of age to insensible perspiration and metabolism, measured with the balance and respiration chamber, respectively. The crosses indicate the average points from which the smoothed curves were constructed.

correlation between the two variables demonstrable in simultaneous measurements. The homogeneous character of these published data for basal metabolism and basal insensible perspiration of normal infants[6] made them available for the present purposes of correlation.

The results are graphically presented in the form of charts of correlation. Charts 2, 3, 4 and 5 present smoothed curves showing the trend of both basal metabolism and basal insensible perspiration of

normal infants referred to age, weight, height and surface area, respectively. The curves for metabolism were constructed from the published figures of Benedict and Talbot;[8] those for insensible loss were taken from the last paper of this series.[1] Both series of smoothed curves were laid out according to standard statistical methods.[16] Only the averaged points used in the construction of each curve are shown in the respective charts. One gram of insensible perspiration per hour was made to equal 50 calories of heat per twenty-four hours in the preparation of the charts.[18]

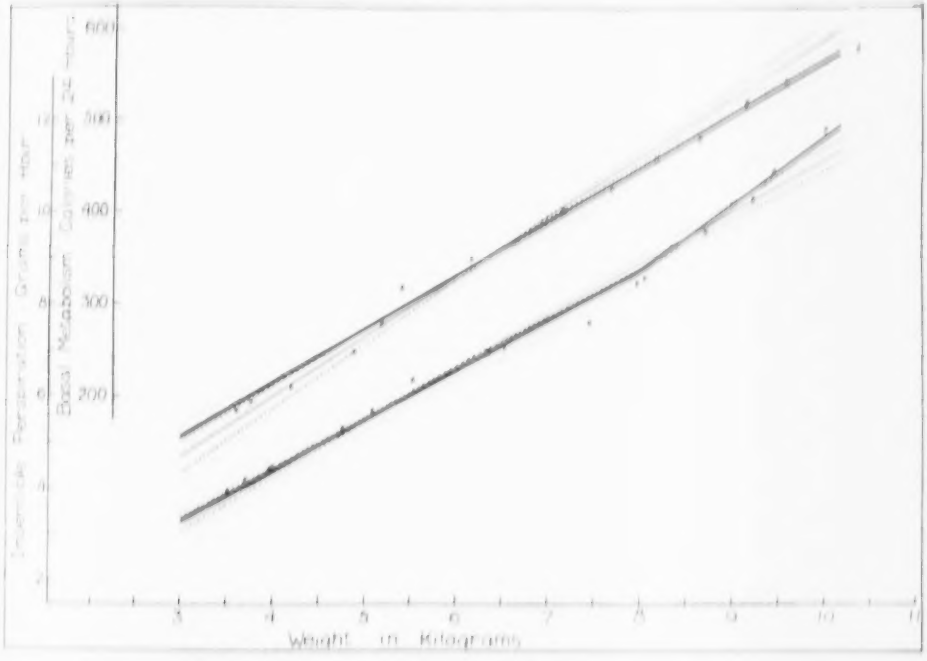

Chart 3.—Relationship in infants of weight to insensible perspiration and metabolism, measured with the balance and respiration chamber, respectively. The smoothed curves were constructed as in chart 2. The broken and the light continuous lines represent the theoretical regression and the theoretical mean regression curves, respectively. The same method of presentation was followed in charts 4 and 5.

18. These values were selected for purposes of correlation on the basis of the data presented in chart 1 and because they represent the relation which exists in normal infants between the generally accepted standards for their basal metabolism and the recently proposed standards for their basal insensible loss as measured with the balance (footnote 1). For infants less than 1 year of age, the respective average figures are 50 calories per kilogram of body weight per twenty-four hours and 1 Gm. per kilogram of weight per hour. This relationship is maintained in older infants, but measurements of the insensible loss with the balance are not as yet available for older children.

The charts are for the most part self-explanatory. For the present purposes, they need be considered only so far as they bear on the reliability of the individual smoothed curves for metabolism and insensible perspiration and on the correlation between the two sets of curves. A detailed discussion of the specific effects of age and size on the individual mechanisms of heat production and insensible perspiration is unnecessary, since this phase of the subject has been amply reviewed in previous papers.

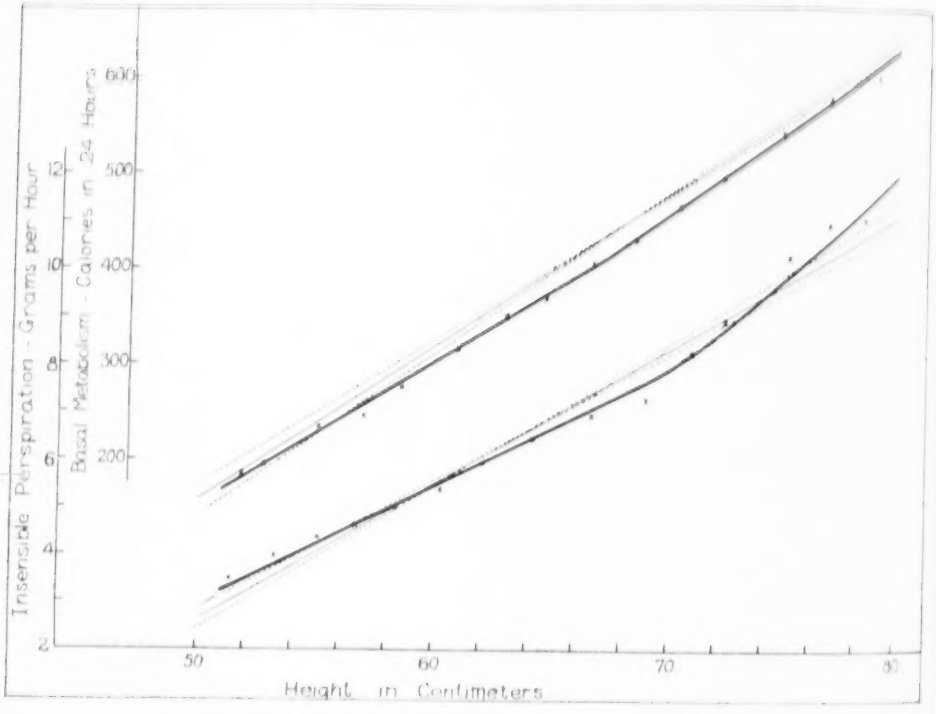

Chart 4.—Relationship in infants of stature to insensible perspiration and metabolism, measured with the balance and respiration chamber, respectively.

A striking parallelism between the curves of basal metabolism and basal insensible perspiration is apparent in all of the charts. In chart 1, the smoothed curves showing the trend of the two measurements with increasing age tend to flatten out in the region of about 1 year, but the parallelism between them is well maintained. In the last three charts, the parallelism between the curves is likewise evident, but a slight disparity in the appearance of the individual curves is noticeable in the regions encompassing infants of approximately 8 Kg. in weight and

in infants of equivalent height (70 cm.) and surface area (0.37 sq. m.) The curves for insensible loss show a slight degree of angling in these zones, whereas the curves for metabolism are straight lines in the charts. This discrepancy may indicate a true difference of functioning of the two mechanisms at this level, or it may depend primarily on the few observations thus far available for insensible perspiration in this region. Information pertaining to these alternative suppositions seemed

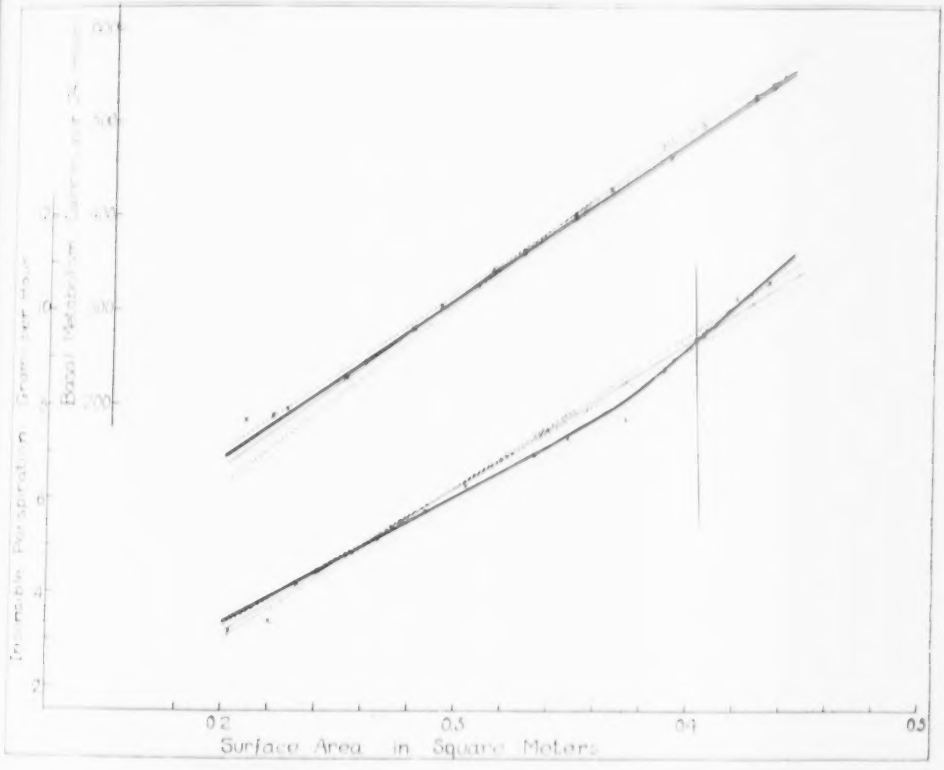

Chart 5.—Relationship in infants of surface area insensible perspiration and metabolism, measured with the balance and respiration chamber, respectively.

best obtained by the application of statistical methods to the observed data for insensible loss. A brief summary of the results of this treatment appears in table 3.

The evidence presented in this table proves that the relationship between basal insensible perspiration and the variables, weight, surface area and probably height, is in every instance a linear equation and may, therefore, be represented graphically by a straight line curve. The

relationship between age and insensible loss on the other hand is a non-linear one [18] and is so illustrated by the smoothed curve in chart 1.

The proved linear character of the correlation indicates that the slight angling visible in the smoothed curves for insensible perspiration and weight, height and surface area shown in charts 3, 4, and 5 depends almost certainly on insufficiency of observed data. It is likely that with the accumulation of more material, these observed curves will take the form of straight lines. The obvious linear relationship between basal

TABLE 3.—*Statistical Constants Indicating the Type of Correlation Between Insensible Perspiration and Physical Factors* *

Variables	Coefficient of Correlation γ_{xy}	Ratios of Correlation η_{xy}	Ratios of Correlation η_{yx}	ζ_{xy} $(\eta_{xy})^2 - (\gamma_{xy})^2$	ζ_{yx} $(\eta_{yx})^2 - (\gamma_{xy})^2$
Insensible perspiration (x)					
Height (y)	0.0458 ± 0.0077	0.0520	0.0603	0.0146 ± 0.0174	0.0400 ± 0.0187
Weight (y)	0.0510 ± 0.0068	0.0615	0.0667	0.0200 ± 0.0200	0.0389 ± 0.0241
Surface area (y)	0.0578 ± 0.0059	0.0705	0.0689	0.0255 ± 0.0225	0.0248 ± 0.0230
Age (y)	0.0091 ± 0.0138	0.0550	0.0581	0.0078 ± 0.0413	0.0348 ± 0.0303

* A correlation is linear when the coefficient and ratios of correlation (γ_{xy}, η_{xy} and η_{yx}) are of approximately similar magnitude and when, furthermore, differences of the squares of the above constants (ζ_{xy}, ζ_{yx}) are not significantly greater than their probable errors (footnote 16).

TABLE 4.—*Calculated Regression Formulas* *

Surface area (y)		
Metabolism (x)	$x = 1656.6\,y - 177.4$	$y = 0.00052\,x + 0.1401$
Insensible loss (x)	$x = 29.36\,y - 2.551$	$y = 0.0312\,x + 0.1049$
Weight (y)		
Metabolism (x)	$x = 50.68\,y - 25.96$	$y = 0.0144\,x + 1.307$
Insensible loss (x)	$x = 1.066\,y + 0.211$	$y = 0.849\,x + 0.371$
Height (y)		
Metabolism (x)	$x = 15.12\,y - 981.9$	$y = 0.069\,x + 41.07$
Insensible loss (x)	$x = 0.2664\,y - 10.448$	$y = 3.393\,x + 41.782$

* Regression lines were not calculated for metabolism or insensible perspiration and weight since they are nonlinear equations (table 3).

metabolism and weight, height and surface area (charts 3, 4 and 5) eliminated the necessity of statistical treatment of these variables.

The evidence of linear correlation already mentioned made it possible to construct theoretical regression curves for both basal metabolism and insensible perspiration and the factors of weight, height and surface area. The formulas employed in their construction are shown in table 4 (derivation of formulas in table 2).

19. These statements are based on the following axiom. In statistical work, an equation is linear when the ratios of correlation ($\eta\,xy$, $\eta\,yx$) and the coefficient of correlation ($\gamma\,xy$) between the two variables are of approximately similar magnitude and when, furthermore, differences between the squares of these constants ($\zeta\,xy$, $\zeta\,yx$) are not significantly greater than their probable errors. The converse is also true (footnote 16).

Superposition of the regression curves (in broken lines) on the observed curves for metabolism and insensible loss in charts 3, 4 and 5 shows clearly the identity of the slopes of the two series of curves. The regression curves calculated for insensible loss eliminate the angling previously mentioned and almost completely correct the minor disparity between the observed curves for metabolism and insensible loss visible in the charts.

The results of the statistical analysis may be accepted as affording satisfactory evidence of correlation in normal infants between basal

TABLE 5.—*Metabolic Equivalents for Given Values of Insensible Loss Derived from Observed and Mean Regression Curves*

Insensible Perspiration, Gm. per Hour	Metabolism, Calories per 24 Hours	
	From Observed Curves	From Regression Curves
	For Age (chart 2)	
4	392	*
6	508	
8	455	
10	593	
11	698	
	For Height (chart 4)	
4	513	555
6	558	547
8	465	465
10	590	575
	For Weight (chart 3)	
4	105	180
6	303	295
8	410	410
10	500	525
	For Surface Area (chart 5)	
4	182	182
6	310	300
8	430	417
10	510	530

* Regression curves for the variables and age were not constructed since the relation between them is represented by nonlinear equations (table 3).

metabolism and basal insensible perspiration as measured with the respiration chamber and balance, respectively.

Prediction of the Metabolism of Infants from Their Measured Insensible Perspiration.—A preliminary tabulation was made of the metabolic equivalents of insensible loss obtained from each of the seven pairs of mean regression or observed curves shown in charts 2, 3, 4 and 5 as an aid in the selection of the most representative figures for prediction purposes.

Table 5 shows that the metabolic equivalents for a given insensible loss vary to some extent when computed from the different curves. When prediction is based on the observed curves for age and height and on the mean regression curves for height (charts 2 and 4), the metabolic rate is fixed at a constant but higher level than when the bases

of prediction are the mean regression and observed curves for weight and surface area (charts 3 and 5). In the latter instances, the metabolic rate is also constant. It seemed preferable to select the curves based on weight and surface area rather than those based on age and height for purposes of prediction, since the standards for the basal metabolism of infants that are generally accepted are those referred to the former factors, and since the highest coefficients of correlation were obtained between basal insensible perspiration and the same factors (table 1). Composite curves of correlation, therefore, were constructed from the

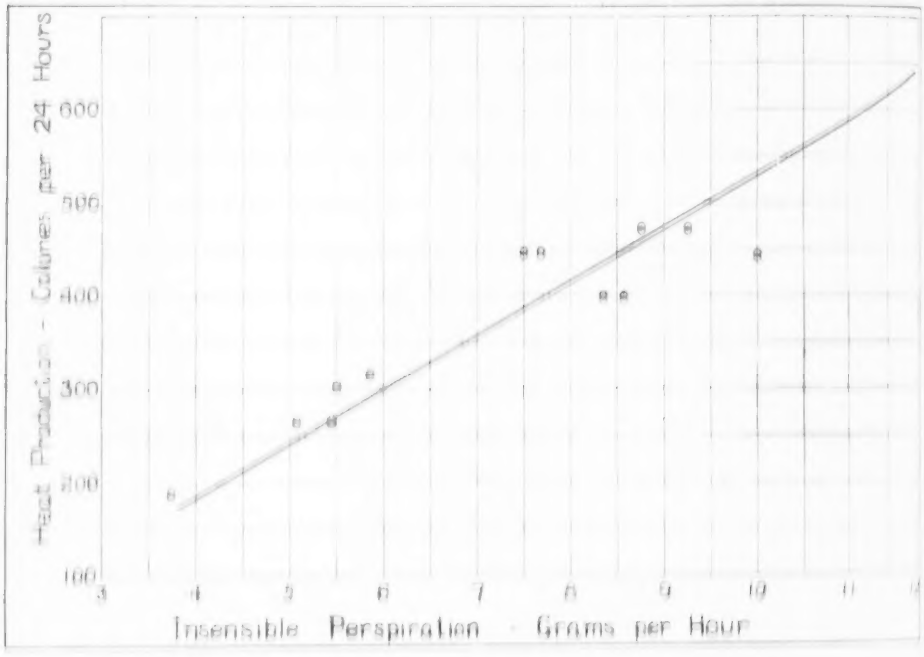

Chart 6.—Proposed curve for predicting the heat production of infants from their insensible perspiration measured with the balance. The circles represent actual measurements in infants of metabolism and insensible perspiration with the respiration chamber and balance, respectively.

four pairs of curves referred to weight and surface area. It is obvious from the figures given in table 5 that the slope of all of these curves coincides. This is true whether the mean regression curves or observed curves for basal metabolism and basal insensible perspiration referred to weight or surface area are used. For purposes of clarity, however, only the composite curve of correlation derived from the mean regression lines for these variables referred to surface area is shown in chart 6. This curve is presented as a tentative method of predicting the

metabolism of infants from their insensible perspiration measured by the simple method of weighing.

The following observations were made to control experimentally the reliability of the proposed curve as a method of prediction: The insensible loss of eight infants was measured with the balance in twelve basal observations, and on the same or the following day their heat production was determined in the respiration chamber under comparable conditions. The infants comprised three subjects in good nutrition, four in poor nutrition and one with cretinism. The results are graphically shown in chart 6. Each point represents the measured insensible loss of an infant with the balance and his determined metabolism in the respiration chamber. One notes that the scatter of these points approximates the prediction curve as laid out, and that only one of the points exceeds a deviation of ± 15 per cent. The percentage deviation of the predicted from the actually determined metabolic values averages -1 per cent for the whole series.

The relatively small series of infants thus far studied jointly by the two methods indicate the advisability of combined studies on a larger series of infants to check the validity of the proposed prediction curve. It is of interest to note, however, in this connection that the present group of infants included subjects showing an abnormal respiratory exchange and that application of the curve proved satisfactory for prediction in these subjects. It must be emphasized that although the statistical evidence of correlation between metabolism and insensible perspiration is conclusive, and although this evidence is confirmed by the results obtained in successive measurements of the two variables with the balance and respiration chamber, respectively, in a small series of infants, the proposed curve of prediction is tentative and may need revision with the accumulation of additional data.

SUMMARY AND CONCLUSIONS

A statistical study was made of the published data responsible for the standards at present available for the basal metabolism and basal insensible perspiration of normal infants. A similar study of statistical and experimental nature was also made of the correlation between the two variables in simultaneous calorimetric measurements as well as in independent measurements with the respiration chamber and balance, respectively.

The results verify, by statistical methods, the validity of the tentative standards recently proposed for the basal insensible perspiration of normal infants [1] and indicate that they compare favorably in reliability with the generally accepted standards for the basal metabolism of these subjects.

The evidence, statistical and experimental, also establishes a high positive correlation between the physiologic mechanisms of heat production and insensible perspiration in the human subject, whether measured simultaneously in the respiration chamber or independently with the balance and respiration chamber. Evidence of correlation between the two variables in independent measurements is thus far limited to infants and adults.[7]

The demonstration of causal relationship in infants between the two mechanisms was utilized to extend to these subjects the method proposed by Benedict and Root for predicting the probable metabolism of adults from their insensible perspiration measured with a balance. This method gave satisfactory results in the small number of infants thus far studied. The latter included several subjects with an abnormal respiratory exchange. The proposed method of prediction is at present limited to infants studied under basal conditions, but it is probably applicable to other than basal conditions so long as visible perspiration is not present and in the absence of derangement of the water metabolism. In our clinic this method is being used at the present time for estimating the basal metabolism of infants, and it is recommended for clinical purposes.

161 West Sixty-First Street.

NUTRITION OF CHILDREN ON A MIXED AND ON A VEGETABLE DIET*

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Many investigators in the science of nutrition have demonstrated that in certain animals the rate of growth and the size can be influenced through the choice of foods, irrespective of heredity and environment. With the rapid progress in the study of foods along this line, various experiments on the growth of children have been undertaken, and much has been said concerning the "normal" rates of growth.

Several standards are now employed for these "normal" calculations, but a student of a critical mind must necessarily question the accuracy of the "normal," since many factors must be involved in drawing a conclusion. Generally and for the most part, the "normal" has been applied merely to the rate of growth in body weight compatible with a given height and age. For a number of years it has appeared to one of us (D. E. L.) that overemphasis has been placed on this phase of "normal" development, for there appear other factors of equal importance in making standards of child health, including resistance to infections, overcoming development of organic diseases, endurance and mentality, the sum of all data indicating the desirability of any choice of foods. Many investigations have demonstrated interesting data on these phases of life, without special reference to standards of growth.

It is gratifying to learn that investigators are gradually realizing that weight, height and age calculations may have serious limitations, and that they are coming more and more to employ other criteria for evaluating the "normal" development of children. In 1922,[1] one of us (D. E. L.) published the results of some clinical experience with these ideas in mind, hoping to stimulate interest and questions, with the view to carrying out controlled experiments at some future time.

During the last two years this plan, as far as it has gone, has met with success in the conducting of two experiments in child feeding. One includes a study in the nutrition of pregnancy, lactation and infancy, which will be published later; the other deals with the nutrition of a group of children from 7 to 15 years of age, and forms the basis of this paper.

* Submitted for publication, Feb. 19, 1930.

1. Lane, D. E.: Nutrition and Specific Therapy, New York, The Macmillan Company, 1922.

The purpose of this investigation was to determine the effect of a combination of vegetable foods which had been tested in a clinical manner by one of us (D. E. L.) since 1918, as compared with the effect of the ordinary milk, meat, bread and vegetable diet on the general health of growing children from 7 to 15 years of age.

REVIEW OF LITERATURE

In 1922, Sherman and Hawley[2] conducted certain balance experiments on children to determine calcium and phosphorus storage, and found that children from 3 to 13 years old on an ordinary mixed diet containing daily 750 Gm. of milk stored from 0.15 to 0.62 Gm. of calcium a day. When the daily allowance of milk was increased to 1,000 Gm., the calcium storage was materially increased.

In another series of experiments these investigators planned to ascertain whether children utilize the calcium of vegetables as well as that of milk. The results of several experiments indicated that calcium storage fell when the amount of milk was reduced. Conclusions were drawn that "one quart of milk per child per day is the amount required for optimum storage of calcium, and presumably, therefore, for optimum development of bones and teeth. . . . Repeated experiments under varied conditions indicate children do not utilize the calcium of vegetables as efficiently as they do that of milk."

In the face of clinical observations, these conclusions have seemed to raise several questions. It has become increasingly evident that certain vegetable foods have a greater biologic value for calcium and phosphorus storage and for general health than others, and that possibly, therefore, the vegetables used by Sherman and Hawley were inadequate in kind and amount. The acid-base equilibrium of the blood may have been at fault, and the ratio of certain mineral elements, for example, calcium and phosphorus, may have been displaced.[3] The vitamins provided by the vegetables did not appear generous in amounts, both because of the kinds of foods used and their preparation. The reaction of the intestines does not seem to have been considered.

The diets of Sherman and Hawley were much more acid-forming than the diet used in the experiment here described. In our experimental diet we did not use macaroni, spinach or prunes; we used very little oatmeal and no meat. Cow's milk is regarded as neutral, but in metabolism it may be slightly acid-forming because of defective absorption of base-forming elements. We used far more orange juice and other raw basic foods and a large quantity of almonds and figs. Our

2. Sherman, H. C., and Hawley, Edith: Calcium and Phosphorus Metabolism in Childhood, J. Biol. Chem. **53**:375 (Aug.) 1922.

3. Shohl, A. T., and Bennett, H. B.: Rickets in Dogs: Metabolism of Calcium and Phosphorus, J. Biol. Chem. **76**:633 (March) 1928.

experimental diet was much more laxative, and the reaction of the intestines was probably more acid, insuring better mineral absorption.

Another noteworthy experiment along this line was made by Newell and Miller,[4] in 1923, with 45 cc. of orange juice added to the diet of fourteen children; this produced considerable gain.

In the same year, Chaney [5] carried out experiments with orange juice in place of milk as supplementary feeding for school children. She found that milk and oranges taken at the same time appeared to stimulate growth at a level slightly higher than milk or orangeade alone, but not as much as do oranges alone.

In 1925, Chaney and Blunt [6] continued this experiment, and found that not only calcium, but also phosphorus, magnesium and nitrogen were better retained when from 600 to 700 cc. of orange juice were added to the mixed milk diet which contained about one-half pint of milk. A marked increase in the children's weight was observed.

In 1926, Morgan and Hatfield [7] conducted supplementary diets with milk, orange juice and figs, and these fruits also gave favorable results. Thirteen children were given one-half pint of milk each a day as supplementary lunch, thirteen were given one medium large orange each, ten were given four pulled figs each and eleven were used as controls. Judged by the Baldwin-Wood standard of nutrition, following fourteen weeks of supplementary feeding, the children in the milk, orange and fig groups had made almost exactly the same amount of improvement. An average of all the gains by different standards showed the orange group to be first, the fig and milk group next and the control group last. The gross average gain in pounds was largest for the milk group, and the average percentage gain in weight above that expected according to the Holt standard was largest for the orange and milk groups. The greatest gains in chest circumference were made by the fig group.

In the same year, Morgan and Hatfield [8] conducted experiments on the effect of various supplementary lunches on the plasma carbon dioxide

4. Newell, F., and Miller, E. W.: The Effect of Adding Orange Juice to the Diets of Underweight Children, J. Home Econ. **15**:241, 1923.

5. Chaney, M. S.: A Comparison of the Value of Milk and Oranges as Supplementary Lunch for Underweight Children, Am. J. Dis. Child. **26**:337 (Oct.) 1923.

6. Chaney, M. S., and Blunt, K.: The Effect of Orange Juice on the Calcium, Phosphorus, Magnesium and Nitrogen Retention and Urinary Organic Acids of Growing Children, J. Biol. Chem. **66**:829 (Dec.) 1925.

7. Morgan, A. F., and Hatfield, G. D.: A Comparison of the Effects of Supplementary Feeding of Fruits and Milk on the Growth of Children, Am. J. Dis. Child. **32**:839 (Dec.) 1926.

8. Morgan, A. F., and Hatfield, G. D.: The Effect of Various Supplementary Lunches on the Plasma Carbon Dioxide Capacity of Children, Am. J. Dis. Child. **32**:655 (Nov.) 1926.

capacity of children. Most of the subjects fed orange juice showed increases in alkaline reserve of from 4 to 9 per cent. On changing from oranges to milk, there was a definite decrease in the alkaline reserve. One child who was given figs gained more than three times the expected amount in weight and showed an increase of 5.5 per cent in carbon dioxide-combining power of the plasma after an interval of forty-three days. Five children who were given oranges as a supplementary lunch showed increases in carbon dioxide-combining power of the plasma of from 1.7 to 11.19 per cent. Two subjects who failed to make the expected gain in weight also showed the lowest gain in alkaline reserve.

In 1923, Hindhede[9] published his study of "Eden" settlement in Germany, composed of 180 families. The people lived on the products of the garden, supplemented with bread, flour, groats and margarine. Milk was used "very sparingly," less than a glass a day. The development of the children was "above the normal" and "during the 25 years the Eden school had existed, not one school child had died."

There are several recent papers[10] dealing with milkless diets for nursing infants and lactating mothers. The results were favorable, provided the diet included suitable and adequate supplementary food other than milk. In his experiment, Ernest Tso[11] found a mild degree of rickets which was not controlled by cod liver oil alone or by any other antirachitic agency.

Following the publication of these results, Hill and Stuart,[12] in this country, have prepared a vegetable milk for infants for whom cow's milk is contraindicated. They do not state that it is as good as cow's milk, but as far as the results indicate, the product appears to give entire satisfaction.

The results of these several researches are in harmony with studies of this character begun by one of us (D. E. L.) in April, 1928,[13] which appear to present even stronger proof of the "entire satisfaction" obtained from this type of feeding, not as a cow's milk substitute, but as food to be used in preference to it over a long period.

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9. Hindhede, M.: Havebrugskolonien "Eden," 19th Report, 1923.

10. Tso, Ernest: Chinese J. Physiol. **2**:33 (Jan.) 1928. Appleton, V. B.: Effects of High Cereal Diet on the Growth of Infants, Am. J. Dis. Child. **37**:284 (Feb.) 1929. Abraham, G.: Milkless Diet in Infancy, Arch. f. Kinderh. **84**:1 (April) 1928. Hill, L. B., and Stuart, H. C.: A Soy Bean Preparation for Feeding Infants with Milk Idiosyncrasy, J. A. M. A. **93**:985 (Sept. 28) 1929.

11. Tso (footnote 10, first reference).

12. Hill and Stuart (footnote 10, fourth reference).

13. Data to be published.

In China, Appleton [14] stated that one is struck by the fine physique, excellent teeth, strength and endurance of the coolies who have never tasted milk, and who live on a diet in which rice furnishes a large proportion of the caloric intake.

In an editorial appearing in 1925,[15] it is stated: "We have become accustomed to emphasize the desirability of milk and dairy foods to supplement the indispensable element calcium, for example. How about those parts of the world in which milk is a luxury, if indeed it is available at all? . . . it is scarcely believable that great groups such as the Chinese, the Japanese or the inhabitants of Indian provinces, exist continually under serious dietary handicaps when the survival of such vigorous races is contemplated." Wheat predominates in the diet of north China. "Milk is scarcely ever used, and meat does not enter in large amounts. . . . We are not wont to consume an equally bulky diet . . . but the maintenance of health and vigor on diets widely different from our own should warn us against extreme deductions."

There is no question but that these people survive under certain dietary handicaps; however, there seems to be no proof that a calcium deficiency is included. There is increasing clinical evidence that strong healthy teeth may be produced, regardless of their care, when diets are largely or entirely composed of vegetable foods,[16] and that dental caries can be completely arrested by suitable, adequate combinations of foods, regardless of the reaction of the saliva or the bacteria in the mouth.

In animal experimentation, some interesting papers have appeared by Cowgill, Jones, Frisch and Jackson.[17] The conclusion is drawn that when suitable, adequate supplementary foods are employed with whole grain cereals, these supplements, contrary to the current belief, need not include milk for growth, reproduction and lactation.

A recent study bearing on this problem is reported by Mayer and Kugelmass,[18] since it discusses the influence of the acid and base-forming diets on various phases of general health. The conclusion is

14. Appleton (footnote 10, second reference).

15. Diet in China, editorial, J. A. M. A. **84**:517 (Feb. 14) 1925.

16. Kappes, Louise O.: Factors in the Decay of Teeth, Am. J. Dis. Child. **36**:368 (Aug.) 1928. Boyd, J. D.; Drain, C. L., and Nelson, M. V.: Dietary Control of Dental Caries, Am. J. Dis. Child. **38**:721 (Oct.) 1929. Additional data is to be published.

17. Cowgill, G. R.; Jones, M. H.; Frisch, R. A., and Jackson, G. P.: Studies on the Effects of Abundant Cereal Intake: I. The Use of Cereals as the Chief Source of Calories, J. A. M. A. **89**:1770 (Nov. 17) 1927; II. The Use of Supplements Other than Milk, ibid. **89**:1930 (Dec. 3) 1927.

18. Mayer, E., and Kugelmass, I. N.: Basic (Vitamin) Feeding in Tuberculosis, J. A. M. A. **93**:1850 (Dec. 14) 1929.

drawn from experiments on rats that a basic diet, high in vitamins, produces better bone formation, greater gain in weight, firmer muscle, healthier fur, more vigorous activity, better appetite, more normal stools, greater resistance to disease and more normal reproduction than an acid-forming diet. A similar experiment is reported by Samuel and Kugelmass[19] with favorable results from the base-forming feeding.

ADVANTAGES AND DISADVANTAGES OF MILK AS FOOD

In the study of the dietary properties of foods, milk has long occupied the center of attention. Its use unquestionably presents many advantages, but it must be admitted that there are likewise disadvantages. The protein is of fairly good quality, the fat is easily digested, and the carbohydrate is readily utilized and encourages the growth of lactic acid-forming bacteria in the intestines. The necessary minerals are well represented in milk ash, especially calcium and phosphorus, and vitamin A is adequately supplied when the milk fat is used. Milk is an easy food to serve. However, the biologic quality of the protein is not the best, although generally looked on as superior to most proteins of vegetable origin. The nutritive ratio is excessively high. Milk is low in iron, iodine and copper, and other minerals are not well balanced for the human organism. Vitamins B and C are often deficient, and D is questionably represented. Milk is lacking in unabsorbable material and as likely to produce constipation as not. Its buffer substances may interfere with gastric digestion and with absorption in the intestines. It is very satisfying, and therefore children especially often will not eat a sufficient amount of other necessary foods when milk is given. Many infants and children cannot tolerate milk.

In spite of a glass of milk with every meal and other well chosen foods, many children at an early age are frequent victims of common colds, diseased tonsils, adenoids, decayed teeth and various common infections and glandular diseases. The question is still unanswered as to whether these misfortunes might not be largely controlled by some other combinations of food furnishing the nutrients in a normal ratio for growth and health. However, this normal ratio cannot be discovered until much more is known of the biochemistry of the normal human organism. Nevertheless, in the meantime progress may be made in eliminating, overcoming and alleviating disease through the clinical testing of improvements on traditional diets.

Hamilton and Moriarty,[20] in discussing milk feeding, have said that, "the large excess of calcium intake may possibly obscure the funda-

19. Samuel, E. L., and Kugelmass, I. N.: Influence of Acid and Base-Forming Feeding on Growth, Proc. Soc. Exper. Biol. & Med. **27**:195 (Dec.) 1929.

20. Hamilton, Bergt; and Moriarty, Margaret: Factors Influencing the Excretion of Calcium, Am. J. Dis. Child. **36**:451 (Sept.) 1928.

mental laws of calcium metabolism, and as cow's milk also in many other respects constitutes an abnormal food, it is conceivable that adjustments are taking place in the metabolism, making the picture less clear."

Furthermore, as Hess and Lewis [21] have pointed out, normal calcium and phosphorus retention are not necessarily a guarantee against disease caused by a deficiency of these minerals, since they find that rickets may develop even when the blood calcium and phosphorus are at the normal level.

EXPERIMENTAL WORK

With the cooperation of Prof. Agnes Fay Morgan of the Department of Household Science, University of California, we obtained permission to carry on the study at the Fred Finch Orphanage in Oakland, Calif. The feeding was begun on May 31, 1929, and continued for ten weeks.

Twenty-six undernourished children were selected, from 7 to 15 years old, thirteen of whom were placed in the control group and thirteen in the experimental group. In the course of the experiment, one of the subjects in the experimental group left the orphanage. Two children in the experimental group and four children in the control group visited relatives for a number of days during the period of observation. Although the children were given the special foods to take with them, and they promised to adhere to the diet while away, some irregularities may have occurred. Another complication was a camping vacation for the whole group of children in the middle of June for three weeks, which somewhat interfered with the food plan for both groups.

Measurements.—The children in each group were examined in regard to firmness of muscle, weight, height, condition of the skin, mucous membrane, hair and eyes, circles under the eyes, facial expression, posture, disposition, animal spirits, constipation, alveolar carbon dioxide, hemoglobin, strength of hand grip estimated by the dynamometer, circumference of chest, expansion of chest, urine P_H and basal metabolism.

The standards for basal metabolism used were taken from Benedict and Talbot's tables [22] in calories per square meter of the body surface varying according to age. Basal metabolic records were made with the portable Benedict apparatus with a kymograph record of oxygen retention at the beginning and at the end of the experiment, and the results were checked in duplicate.

Underweight and overweight were calculated according to the weight-height-age tables for boys and girls by Baldwin and Wood. Age was taken at the nearest birthday, height at the nearest half inch and weight at the nearest half pound.

Carbon dioxide was determined by the method of Marriott.[23] According to Marriott's standards for children from 11 to 13 years old, from 35 to 40 mm. of

21. Hess, A. F.; Lewis, J. M., and Rivkin, Helen: The Status of the Therapeutics of Irradiated Ergosterol, J. A. M. A. **93**:1661 (Aug. 31) 1929.

22. Benedict, F. G., and Talbot, F. B.: Basal Metabolism and Growth from Birth to Puberty, Carnegie Institution, Washington, 1921.

23. Marriott, W. M.: The Determination of Alveolar Carbon Dioxide Tension by a Simple Method, J. A. M. A. **66**:1594 (May 20) 1916.

mercury is considered normal, from 25 to 30 mm., as showing mild acidosis and below 20, serious acidosis. Hemoglobin was determined by the Tallquist method, and urinary p_H by the colorimetric method of Henderson and Palmer.

Diets.—In the control group, the aim was to prepare what has been considered the normal conservative mixed diet, balanced in all respects as scientifically as possible in the light of present knowledge of nutrition. The regular orphanage diet was taken as a basis, and the necessary additions were made. The children were receiving ample amounts of meat, eggs, potatoes, cereals and bread and rather moderate amounts of milk, butter, fruits and vegetables. Therefore, the milk was increased to one cup at each meal, and since they received milk on their cereal, in cocoa and in cooked foods, it was considered that each of the thirteen children received the "required" quart of milk a day. The fruits and vegetables were both increased in the form of salads, hot vegetables and fresh fruits. Cheese was often included in the evening meal.

TABLE 1.—*Typical Day's Dietary of Milk Control Group*

Meal	Food	Calories	Protein, Gm.	Calcium, Gm.
Breakfast:	Milk in postum, ⅝ cup	100	4.75	0.174
	Oatmeal, ½ cup	50	2.10	0.008
	Milk on cereal, ¼ cup	50	2.37	0.087
	Butter, 1 square	50	0.06	0.001
	Stewed peaches	100	1.70	0.038
	Toast, 2 slices	100	3.95	0.020
	Sugar, 2 teaspoonfuls	33	....	.....
		483	14.93	0.328
Lunch:	Milk, 1 cup	140	6.65	0.243
	Bread, 2 slices	100	3.95	0.020
	Butter, 1 square	50	0.06	0.001
	Vegetable soup	100	2.27	0.030
	Apple	100	0.64	0.012
		490	13.57	0.306
Dinner:	Braised beef, 3½ ounces	165	12.12	0.006
	Baked potato, 4 ounces	100	2.65	0.016
	Bread, 2 slices	100	3.95	0.020
	Butter, 1 square	50	0.06	0.001
	Cabbage and carrot salad, 3½ ounces	75	1.10	0.067
	Milk, 1 cup	140	6.65	0.243
	Banana	100	1.32	0.009
		730	27.85	0.362
Day's total		1,703	56.35	0.996

In the experimental group, no milk, cream, cheese, eggs or meat was given and very little butter, the same amount as furnished in the control group. Instead, almonds were given for their basicity, calcium, iron, copper and protein; wheat germ for the vitamin B complex, calcium, phosphorus, iron, iodine, copper and protein; figs for their basicity, calcium and iron and their laxative property, and a cup of orange juice at each meal for its basicity, calcium and vitamins A, B and C. Peanut butter, valuable for its basic amino-acids, and other legumes were also included. Only a small amount of commercial cane sugar was allowed, but honey was used freely for sweetening.

For both groups the vegetables included much raw cabbage, lettuce and carrots, and considerable amounts of cooked string-beans. No spinach was given in the experimental group, since the metabolism of its oxalic acid is open to question. Aside from the dried figs and orange juice used in the experimental group, the fruits served in both groups included stewed peaches, apricots and raisins, cooked

and raw apples and a good quantity of bananas and tomatoes. Each child in the control group averaged one orange a day, while each child in the experimental group averaged the juice of from eight to nine oranges of medium size (three cups). Potatoes, salads and legumes were served to both groups at the same time, but often the legumes left over were used in another meal for the experimental group. There was a variety of cereals for breakfast for both groups, but the experimental group always had wheat germ and almond meal added in small amounts as one way of serving these two foods. Occasionally, cookies or a simple dessert were given, but the plan was to avoid foods of this character.

The aim in both groups was to furnish approximately 1,750 calories a day per child, although some of the children were smaller than others and so ate less. The protein was calculated as furnishing 10 per cent or more of the calories, and

TABLE 2.—*Typical Day's Dietary of Vegetable Experimental Group*

Meal	Food	Calories	Protein, Gm.	Calcium, Gm.
Breakfast:	Orange juice, 1 cup	100	1.44	0.067
	Oatmeal, ½ cup with ¼ ounce wheat germ uncooked	77	3.90	0.012
	Ground almonds, ½ ounce	40	1.30	0.014
	Honey, ½ ounce	66	0.08	.....
	Stewed peaches	100	1.70	0.038
	Whole wheat toast, 2 slices	100	3.98	0.025
	Butter, 1 square	50	0.06	0.001
		533	12.46	0.157
Luncheon:	Orange juice, 1 cup	100	1.44	0.061
	Whole wheat bread, 2 slices	100	3.98	0.025
	Butter, 1 square	50	0.06	0.001
	Vegetable soup	100	2.27	0.030
	Apple	100	0.64	0.012
	Almonds (14), ½ ounce	80	2.60	0.028
		530	10.99	0.163
Dinner:	Lentil loaf, 3½ ounces	150	11.03	0.046
	Baked potato, 4 ounces	100	2.65	0.016
	Whole wheat bread, 2 slices	100	3.98	0.025
	Butter, 1 square	50	0.06	0.001
	Cabbage and carrot salad, 3½ ounces	75	1.10	0.067
	Orange juice, 1 cup	100	1.44	0.067
	Figs (4), 2 ounces	205	6.61	0.090
		780	26.87	0.312
Day's total		1,843	50.32	0.632

the calcium intake of the experimental group was close to 0.65 Gm. each per day, while that of the control group with the quart of milk averaged 1 Gm. intake.

Cod liver oil was given to six subjects in each group.

COMMENT

The physical appearance of all the children at the end of the feeding period of ten weeks was improved, and this improvement corresponded closely with the gain in the measurements.

In some cases no actual gain in weight or even a loss resulted, but the total net result was usually a gain, for in certain cases of overweight the child was not as much overweight for the height, and other factors showed improvement. Three of the subjects showing loss in weight were in the milk group without cod liver oil.

The greatest average gain in weight of 1.37 pounds was made in the milk group with cod liver oil, but the corresponding gain in height of 0.36 inches was the lowest height average. However, this large gain in weight in this group was almost wholly due to subject 14, who gained 8½ pounds, although the child was ill at the beginning of the experiment with an ear infection. Without the gain made by this subject, the average gain is only 0.51 pounds, which seems a more accurate average for this group. There was a minus average gain of —0.1 pounds in the milk group without cod liver oil. There was a somewhat smaller average gain in weight in the vegetable group with cod liver oil than in the vegetable group without cod liver oil, and the same was true of height in both groups, so no conclusions can be indicated. It may be that the cod liver oil has its greatest effect in increasing the circumference and expansion of the chest, and the hand grip, and possibly also in increasing hemoglobin, with certain foods. It is reasonable to suppose that there is a selective influence of foods combined with cod liver oil.

Subject 15 in the vegetable group with cod liver oil lost 2½ pounds, but was greatly improved otherwise at the close of the experiment. A long-standing enuresis was greatly diminished after eight weeks. Subject 2 in the milk group without cod liver oil was changed from the vegetable group after three weeks because of a rash, possibly due to an idiosyncrasy toward orange juice. This child had gained 2¾ pounds on the vegetable diet, after which there was a loss in weight on the milk diet. Subject 17 in the vegetable cod liver oil group was changed from the milk diet on which there was a continuous loss in weight for four weeks, but on the vegetable diet the loss was more than made up, and the alveolar carbon dioxide and hemoglobin were markedly increased, although because of gain in height this subject was a little more underweight at the end of the period according to the conventional standard. The vegetable group averaged the greater gain in weight, although this gain was slight.

The average gain in weight was probably less for both groups than it would have been during school months, since the children were exceedingly active during the summer. At camp, there resulted a small loss in weight in every child, with the exception of two in the control and two in the experimental group. This fact lowered considerably the final gains in weight. The very small gain and loss in weight in the six children who visited relatives made the resulting error negligible. (Three in the milk group gained, one lost, one in the vegetable group gained and one lost while visiting.)

The progressive gain in the expansion of the chest from the milk group without cod liver oil to the milk group with cod liver oil to the vegetable group without cod liver oil to the vegetable group with cod liver oil may be of significance. This result appears to correspond

TABLE 2.—Physical Measurements of Children at Beginning and End of Ten Weeks' Feeding (May 31 to Aug. 12, 1925)

Subject	Sex*	Age, Yr.	Weight, Pounds: Beginning	Weight, Pounds: End	Height, Inches: Beginning	Height, Inches: End	Underweight, per Cent: Beginning	Underweight, per Cent: End	Overweight, per Cent: Beginning	Overweight, per Cent: End	Hemoglobin, per Cent: Beginning	Hemoglobin, per Cent: End	Alveolar CO_2 Tension, Mm. Hg: Beginning	Alveolar CO_2 Tension, Mm. Hg: End	Hand Grip, Pounds: Beginning	Hand Grip, Pounds: End	Chest Circumference,† Inches: Beginning	Chest Circumference,† Inches: End	Chest Expansion,† Inches: Beginning	Chest Expansion,† Inches: End	Urine, ps: Beginning	Urine, ps: End	Urine, ps: Total Aver.‡
Milk Control Group Without Cod Liver Oil																							
1	♀	12	70.75	81.50	56.25	58.50	.....	.....	12.22	4.55	75	80	37	36	40	46	28.00	28.75	30.25	31.00	5.8	5.0	
2	♀	11	64.50	69.25	54.25	56.13	9.15	7.98	.....	.....	70	80	33	37	40	37	24.25	24.75	26.25	26.75	6.8	6.5	
3	♂	10	56.00	60.25	50.50	51.00	2.22	6.39	.....	.....	70	75	37	37	33	34	25.00	25.00	26.50	26.50	6.6	5.0	
4	♀	9	50.25	52.75	49.25	49.75	.....	4.86	1.36	.....	75	75	33	35	30	30	23.75	23.75	25.50	25.50	6.6	5.6	
5	♀	9	51.25	56.25	49.00	49.75	.....	.....	0.45	0.44	70	80	33	38	29	32	24.50	25.75	25.75	26.00	5.4	6.7	
6	♂	9	61.00	70.00	53.25	56.25	.....	.....	9.45	4.69	75	75	28	32	31	36	26.75	27.00	28.75	29.00	5.9	5.0	
7	♂	9	56.50	59.75	48.75	49.25	.....	.....	5.09	0.28	75	70	36	37	30	32	24.00	24.87	25.37	25.50	5.5	5.9	
Average		9.5	64.42	66.32	51.09	52.18	5.83	7.01	5.73	4.38	72	76	35	36	33	35	25.08	25.35	26.60	27.16	6.1	5.5	5.9
Milk Control Group With Cod Liver Oil																							
8	♂	6	50.25	59.25	48.75	48.50	.....	.....	16.25	11.00	70	70	35	32	24	24	24.25	24.50	25.25	25.50	5.8	5.8	
9	♀	11	77.00	77.25	52.50	52.25	.....	.....	17.80	12.60	65	75	37	32	28	32	27.00	28.25	28.25	29.50	5.4	6.8	
10	♂	10	55.50	59.50	48.75	48.75	.....	.....	7.76	3.70	65	65	37	37	25	31	25.25	25.50	26.25	26.50	5.8	6.0	
11	♂	10	60.00	70.75	52.25	52.50	.....	.....	6.10	0.02	70	75	37	37	30	31	26.00	26.00	26.00	27.00	6.6	5.0	
12	♂	9	56.50	57.50	50.00	50.25	.....	0.86	0.86	.....	70	70	37	32	32	32	26.00	26.25	27.25	27.75	6.7	6.8	
13	♂	10	70.75	75.50	54.25	56.75	.....	.....	6.50	6.50	80	80	30	30	40	40	26.50	27.25	28.50	29.00	7.0	5.9	
14	♂	14	80.00	87.50	60.25	60.25	5.30	.....	.....	7.05	65	95	28	35	48	58	30.00	30.50	32.00	32.00	6.8	5.9	
Average		10	69.25	70.90	51.88	52.32	5.30	0.86	10.10	6.39	73	77	33	33	34	39	26.76	27.26	28.37	28.82	6.2	6.0	6.2
Vegetable Experimental Group With Cod Liver Oil																							
15	♂	6	56.50	59.00	48.50	49.00	.....	.....	7.87	7.81	60	60	35	37	35	35	24.87	24.87	25.37	26.25	5.9	6.8	
16	♀	11	72.50	76.00	55.00	55.50	3.20	1.40	.....	.....	70	70	39	33	36	37	26.50	27.00	28.50	30.00	5.8	6.9	
17	♀	10	66.75	67.00	53.00	53.50	1.85	2.60	.....	.....	70	65	34	40	30	38	26.50	27.00	27.75	28.25	6.6	7.8	
18	♂	10	67.25	69.00	50.50	50.75	.....	.....	9.66	13.38	70	60	35	37	38	38	27.25	27.50	28.25	29.00	5.6	6.7	
19	♀	11	68.50	70.00	54.75	56.25	.....	2.45	1.80	.....	70	80	35	46	30	35	27.75	28.00	29.25	30.25	5.3	6.8	
20	♀	11	104.00	105.50	62.25	62.25	10.58	0.95	.....	.....	65	80	35	35	45	51	30.50	31.00	31.00	31.50	7.0	6.7	
Average		10.0	75.50	77.64	54.33	54.71	5.09	4.75	6.57	6.86	67	72	36	38	39	36	27.25	27.72	28.73	29.64	6.0	7.3	6.9
Vegetable Experimental Group Without Cod Liver Oil																							
21	♀	7	44.0	45.0	46.75	47.50	9.57	11.79	.....	.....	70	70	37	32	17	26	23.00	23.25	24.25	24.75	6.7	7.5	
22	♂	11	60.50	62.00	57.25	57.75	0.61	0.0	.....	.....	70	75	38	32	30	30	27.25	28.25	29.00	30.25	6.8	7.5	
23	♂	11	63.00	70.25	52.25	52.50	.....	.....	1.47	1.45	60	65	36	40	45	44	26.25	26.75	27.50	28.50	6.7	7.1	
24	♀	10	55.75	60.25	50.50	51.25	0.45	1.02	.....	.....	60	60	37	32	34	33	25.00	25.50	27.25	28.50	5.8	6.1	
25	♂	9	51.50	56.0	52.50	53.00	19.07	13.49	.....	.....	70	75	33	37	28	28	25.50	25.50	27.50	27.50	7.0	8.1	
Average		10	62.17	63.55	52.04	52.69	5.62	5.46	1.47	1.45	70	70	36	32	32	35	25.49	25.85	27.39	27.96	6.6	7.2	7.0

* ♀ indicates female; ♂, male.
† Chest circumference and chest expansion taken July 11 and August 12.
‡ Average of five tests, June 9 to Aug. 4, 1925.

with the experiment with figs by Morgan and Hatfield in 1926, in which it was found that the greatest gains in the circumference of the chest were made by the group of children who were fed figs.

The cod liver oil also may possibly have had an influence on the hand grip, but it appears to have had no definite effect on the hemoglobin of the milk group, although there was a large gain in that of the vegetable group. The changes, however, were so small that no conclusion can be drawn. The hemoglobin of both vegetable groups showed definite increases over that of both milk groups.

The gain in the alveolar carbon dioxide in every child in both groups, with the exception of subjects 5 and 7 in the milk group without cod liver oil, was noticeable.

TABLE 4.—*Average Changes in Physical Measurements After Ten Weeks' Feeding*

Diet	Group	Weight, Pounds	Height, Inches	Hemoglobin, per Cent	Alveolar CO_2, Mm. Hg	Hand Grip, Pounds	Chest Circumference, Inches‡	Chest Expansion, Inches‡	Urine, p_H	Number of Children
Milk control without cod liver oil.....	A	−0.10	+0.50	+ 4	+ 6	+ 2	+0.36	+0.58	−0.6	7
Milk control with cod liver oil.....	B	+1.37 (+0.15)*	+0.36	+ 3	+12	+ 5	+0.41	+0.61	−0.2	7
Vegetable experimental without cod liver oil.....	C	+1.18	+0.56	+ 6	+10	+ 2	+0.45	+0.85	+0.6	5
Vegetable experimental with cod liver oil.....	D	+0.50 (+1.10)†	+0.38	+15	+ 9	+ 6	+0.30	+0.89	+1.3	6
Milk control...	A and B	+0.63 (+0.02)*	+0.43	+ 4	+10	+ 4	+0.33	+0.59	−0.4	14
Vegetable experimental....	C and D	+0.84 (+1.14)†	+0.47	+11	+10	+ 4	+0.37	+0.87	+0.9	11

* Average weight change without subject 14 (see comment).
† Average weight change without subject 15 (see comment).
‡ Chest circumferences and chest expansions taken July 11 and August 12.

The final average urine p_H showed a progressive increase in basicity from the milk group without cod liver oil to the milk group with cod liver oil to the vegetable group without the cod liver oil. There was then a slight drop in the basicity of the vegetable group with the cod liver oil, due to subject 18 who ate much bread. Without this subject, the p_H was the same as for the vegetable group without cod liver oil. Since there is some evidence that the acid-base equilibrium of the blood within certain limits has a marked influence on the general health, the question is open as to whether the greater basicity of the vegetable diet (with very high vitamin content) can be credited in any degree with the seemingly beneficial results from this diet.

The data on the basal metabolism will be published later.

The cost of food in the milk and vegetable diets in the majority of localities would average about the same throughout the year. All dairy products, eggs and meats are expensive, and increase food costs about as much as do "juice oranges," bought in quantity, which is the main article of expense in the vegetable diet.

SUMMARY

From the results of this short feeding test there appears no reason to conclude that a scientifically balanced milk diet, including 1½ pints to 1 quart of milk a day per child, produces greater growth or better health in growing children from 7 to 15 years old than a scientifically chosen vegetable diet furnishing a smaller amount of calcium. If there is a greater calcium storage on the milk diet than on the vegetable diet, a supposition which does not appear justified by the gains in height and weight or the other data here presented, there still would seem to be no reason for assuming such excessive storage advantageous for the general health of growing children. Excessive calcium storage may possibly obscure a clear perception of the function of other factors in the diet, whether it be that of the calorie-producing nutrients, the various minerals and vitamins or the acid-base equilibrium of the blood.

A diet of vegetable foods carefully selected with special reference to the quality and quantity of the protein, low in fat, comparatively high in carbohydrate, with adequate amounts of the various minerals and high in vitamins produced in ten weeks as satisfactory increase in all physical measurements observed in children from 7 to 15 years old, and in most cases greater increases, than a similarly carefully planned milk and meat containing diet.

ACUTE OBSTRUCTIVE LARYNGITIS

CLINICAL AND BACTERIOLOGIC STUDY IN SIXTY-SIX CASES *

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The purpose in this paper is to present certain clinical and bacteriologic data concerning a group of children suffering from acute obstructive laryngitis. The material consists of the records of the sixty-six children admitted to the Contagious Service of the Strong Memorial Hospital during the past three years (1926 to 1929) in whom laryngeal obstruction of infectious origin occurred.

While *Bacillus diphtheriae* is the most common cause of this condition, there is no doubt that many cases are diagnosed as laryngeal diphtheria which are actually due to some other organism. The literature concerning nondiphtheritic laryngitis is concerned chiefly with case reports, in many instances of which the bacteriologic data are not complete. The hemolytic streptococcus is frequently cited as the causative organism. Cases due to bacilli of the Friedlander group, to hemolytic staphylococci, to nonhemolytic streptococci and to various organisms have been reported. Baum [1] has given to the nondiphtheritic type of infection an anatomically suitable name, "laryngotracheobronchitis."

The clinical manifestations of diphtheritic and of nondiphtheritic laryngitis are so similar that the actual diagnosis frequently depends on the results of bacteriologic cultures. In these cases differentiation was made chiefly by repeated cultures from the throat and larynx and by direct laryngoscopic examination, and in sixteen of the fatal cases, by anatomic examination.

By such methods of study, our cases fall into two groups: thirty-eight cases of definite laryngeal diphtheria and twenty-eight cases of nondiphtheritic infection. Opportunity, therefore, is afforded (1) to compare the clinical features of the two groups and (2) to present the results of the bacteriologic studies made.

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* Submitted for publication, Feb. 15, 1930.

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1. Baum, H. L.: Acute Laryngotracheobronchitis, J. A. M. A. **91**:1097 (Oct. 13) 1928.

COMPARATIVE CLINICAL STUDY OF THE TWO GROUPS

Age.—The youngest of the diphtheritic group was 7 months of age and the oldest 8 years. The youngest of the nondiphtheritic group was 5 months; the oldest, 13 years. Table 1 gives the age distribution according to years in the two groups.

Sex.—Seventeen males and twenty-one females had laryngeal diphtheria, while among the group of nondiphtheritic infections the males distinctly outnumbered the females, twenty-one to seven; a ratio of 3:1.

Seasonal Incidence.—The diphtheritic cases showed a greater occurrence during the winter and the spring, thirty-five cases occurring between November and May. Most of the nondiphtheritic infections occurred during the spring and the summer, twenty-one of twenty-seven patients being admitted to the hospital between March and August.

Symptoms.—In general, the chief symptoms were similar in the two groups; difficult breathing was the chief complaint in the majority

TABLE 1.—*The Distribution of Cases According to Age*

Age	Diphtheritic	Nondiphtheritic
Under 1 year	3	4
1 to 2 years	6	9
2 to 3 years	4	3
3 to 4 years	10	5
4 to 5 years	10	3
5 to 10 years	5	2
10 to 15 years	0	2

of cases. The chief symptoms and the number of persons manifesting them were as follows: diphtheritic: difficult breathing, thirty-three; cough, twenty-two; fever, thirteen; hoarseness, fourteen; cold, fifteen; croup, eleven; sore throat, eleven; restlessness, six; vomiting, eight; nondiphtheritic: difficult breathing, twenty-five; cough, eighteen; croup, seventeen; fever, seventeen; sore throat, seven; cold, six; restlessness, four; vomiting, nine.

The duration of symptoms before the time of admission was about the same in the two groups, averaging three days in the case of the diphtheritic group, and two and eight-tenths days for the other.

It is interesting to note that the onset of the disease was described as sudden in twenty-one of the twenty-eight nondiphtheritic cases. In about one half of these the onset occurred during the night. In thirty-three of the thirty-eight cases of diphtheria the disease began insidiously. The obstruction was a progressive event in thirty-seven of the diphtheritic cases and in twenty-two of the nondiphtheritic group.

Signs.—Stridor, retraction of the chest with increased respiratory rate, cyanosis and the presence of a membrane were the outstanding signs among the diphtheritic group. The stridor was chiefly of the

inspiratory type and occurred in thirty-seven of the thirty-eight cases. Retraction also occurred in thirty-seven patients, cyanosis in sixteen, enlarged cervical nodes in nineteen and enlarged tonsils in thirty-five. The tonsils were present in each case. On careful inspection, a definite membrane was seen in the throats of thirty-one of the thirty-eight children.

Among the other group, stridor was noted in twenty-eight—in each case of the inspiratory type—cyanosis in nine, retraction in twenty-three, cervical lymphadenopathy in nine and hypertrophied tonsil in fifteen. The tonsils had been removed in four patients. No case revealed a true membrane, although mucoid exudate was noted in the throats of the majority of these patients. Eight of the nondiphtheritic group had previously been immunized by injections of toxin-antitoxin. Five of those with diphtheria had received toxin-antitoxin, but in the case of three the injections were too recent to assure protection.

The average temperature for the diphtheritic group at the time of admission was 38.8 C. (101.8 F.); for the nondiphtheritic group, 38.7 C. (101.6 F.). The average white blood cell counts were 16,770 and 12,700, respectively, with considerable variations in each group.

Direct Laryngoscopic Examination.—Examination of the larynx was made with the laryngoscope in eighteen of the diphtheritic cases. All showed a definite membrane. Thirteen of the second group were examined, and none revealed a membrane. All showed catarrhal inflammation with edema and injection of the mucosa, especially in the subglottic area. Considerable mucus was present in the larynx in these patients.

Intubation.—It is the practice in our service to perform intubation first in all cases of obstruction and to perform tracheotomy later if it is indicated. Thirty-one of the thirty-eight patients with laryngeal diphtheria were intubated. The average length of time during which the tube remained in the larynx was five days. Eighteen of the twenty-eight nondiphtheritic patients were intubated, and it was necessary to keep the tube in place in this group for an average of seven and five-tenths days.

Tracheotomy.—This operation was performed five times among the diphtheritic group. Four patients died, and the one surviving child carried his tube thirty-one days. Among the nondiphtheritic group, tracheotomy was performed on seven; six survived and carried their tubes for an average of thirty-six days.

Mortality.—Twelve (38.7 per cent) of the thirty-one patients with diphtheria, who were intubated, died. Four of these had tracheotomies. Six (33.3 per cent) of the children in the nondiphtheritic group of eighteen intubated died. One of the six having tracheotomy died.

Necropsy.—Ten of the eleven fatal cases of diphtheria and six of the seven nondiphtheritic patients were examined anatomically. In the first group, typical diphtheritic membranes were demonstrated, with the recovery of *Bacillus diphtheriae* in culture in each case. Secondary lobular pneumonia was present in each case. None showed definite myocarditis.

In the nondiphtheritic cases, postmortem examination revealed edema, injection and granulation of the laryngeal and tracheal mucous membranes. No definite membranes were found, but in all cases considerable mucoid exudate was present in the bronchi. Each case presented definite lobular pneumonia. In this group of cases, cultures from the trachea and lungs were negative for *B. diphtheriae*.

BACTERIOLOGY

On the patients' admission to the hospital, swabbings of the throat and nose were cultivated on Loeffler's medium for *B. diphtheriae*. When the first culture was reported negative, another one was taken, and in most cases tube cultures were taken. Cultures were also taken to determine other types of organisms in case the first culture for *B. diphtheriae* was negative. These were taken either as deep throat cultures or, in the cases subjected to direct laryngoscopic examination, directly from the larynx. Tubes of Douglas broth were inoculated, dilutions made, and blood-agar plates poured. After from twenty-four to forty-eight hours' incubation, colonies were counted with special reference to the percentage of hemolytic streptococci and to the predominating organism. In the case of green-producing colonies, representative types were picked and transferred to broth for bile solubility tests and typing in case they were soluble.

Concerning the diphtheria group, it is significant to note that of the thirty-eight cases, the initial culture from the throat was positive in thirty-seven instances. In one case, the first cultures from the nose and throat were negative, but the culture from the tube was positive.

A summary of the bacteriologic reports of the nondiphtheritic group is given in table 2. Table 3 shows the results of the antemortem and of the necropsy cultures in six fatal cases in this group. Among the twenty patients on whom blood-agar pour plate cultures were made, it is evident that the predominating colony was a green-producing streptococcus. The low percentage of hemolytic streptococci is of special interest in these cases in view of the usual opinion that this organism is so frequently found in nondiphtheritic laryngitis. In this series 40 per cent was the greatest proportion found in any case, while the majority of cases ran less than 5 per cent hemolytic streptococcic colonies.

The question naturally arises as to whether or not the green-producing streptococci were capable of producing such severe laryngitis as characterized these cases. Direct evidence on this point is difficult to obtain. Seitz [2] reported a case of obstructive laryngitis in a boy aged 3 years in which *Streptococcus viridans* was the predominating organism

TABLE 2.—*Results of Deep Throat and Laryngeal Cultures in Twenty Cases of Nondiphtheritic Obstructive Laryngitis*

Case	Age	Intubation	Source of Culture	Number of Klebs-Loeffler Cultures Negative	Per Cent Hemolytic Streptococcus	Per Cent Green Streptococcus	Other Organisms Present
P. F.	2 yr.	Yes	Larynx	1	5	90	Pneumococcus type 4
C. B.	2 yr.	Yes	Deep throat	1	10	Predominating	
S. V.	5 mo.	Yes	Deep throat	2	5	60	
J. P.	14 mo.	Yes	Deep throat	1	20	40	Otitis– green streptococcus; M. catarrhalis
H. R.	14 mo.	Yes	Deep throat	3	0	Predominating	M. catarrhalis
H. R.	18 mo.	Yes	Larynx	1	0	Predominating	Staphylococcus albus, M. catarrhalis
G. T.	5 yr.	Yes	Deep throat	1	—1	75	
R. S.	16 mo.	Yes	Larynx	1	—1	Predominating	Staphylococcus albus
L. C.	3 yr.	Yes	Deep throat	1	5	75	
G. M.	4 yr.	Yes	Deep throat	2	0	Predominating	Staphylococcus aureus, Pneumococcus type 4, M. catarrhalis
D. C.	4 yr.	Yes	Deep throat	3	—1	30	Staphylococcus albus
H. W.	10 mo.	Yes	Deep throat	3	40	50	
E. J.	13 yr.	Yes	Larynx	1	0	90	Staphylococcus albus, Pneumococcus type 3
E. R.	13 mo.	No	Deep throat	2	1	75	
M. S.	5 yr.	No	Deep throat	3	1	75	
M. W.	1 yr.	No	Larynx	1	1	90	
J. M.	16 mo.	No	Larynx	1	0	Predominating	M. catarrhalis, Staphylococcus aureus, M. albicans
C. R.	2 yr.	No	Deep throat	1	1	Predominating	Pneumococcus type 4
G. A.	11 yr.	No	Deep throat	2	0	Predominating	Staphylococcus aureus, M. catarrhalis
P. R.	13 mo.	Yes	Larynx	2	0	95	B. influenzae

recovered. Baum [1] found that it was the chief organism in the bronchial secretions in two similar cases. As a result of a small series of cultures from the throats of normal children and of children suffering from acute upper respiratory infections, it was found that green colonies frequently predominated. Six of the green-producing strains recovered

2. Seitz, Roland P.: Acute Streptococcic Laryngitis in Children, California & West. Med. **30**:259 (April) 1929.

TABLE 3.—*Results of Antemortem and of Postmortem Cultures in Six Fatal Cases of Nondiphtheritic Obstructive Laryngitis*

Case	Anatomic Diagnosis	Antemortem Cultures (Throat or Larynx)	Postmortem Cultures		
			Larynx and Trachea	Lungs	Heart's Blood
E. R. 13 mo.	Lobar pneumonia, acute laryngitis	Larynx: Klebs-Loeffler bacillus negative, 1 per cent hemolytic streptococcus, 75 per cent green streptococcus	Klebs-Loeffler bacillus negative (no plate cultures)	Pneumococcus type 3, Staphylococcus aureus, nonhemolytic streptococcus, sarcinae	Streptococcus viridans
P. F. 2 yr.	Bronchopneumonia, acute tracheitis, acute bronchitis	Throat: Klebs-Loeffler bacillus negative, 5 per cent hemolytic streptococcus, 90 per cent green streptococcus, Pneumococcus type 4	Klebs-Loeffler bacillus negative, green streptococcus predominating	Pneumococcus type 4, M. catarrhalis siccus	No growth
P. R. 13 mo.	Bronchopneumonia	Larynx: Klebs-Loeffler bacillus negative, no hemolytic streptococcus, 95 per cent green streptococcus	Klebs-Loeffler bacillus negative, Staphylococcus albus, B. influenzae, green streptococcus	Green streptococcus predominating, Staphylococcus albus	No growth
E. J. 13 yr.	Acute hemorrhagic bronchopneumonia, acute tracheitis, acute laryngitis	Larynx: no hemolytic streptococcus, 90 per cent green streptococcus, Staphylococcus albus, Pneumococcus type 3	Klebs-Loeffler bacillus negative, Staphylococcus albus, green streptococcus, 2 per cent hemolytic streptococcus	Staphylococcus albus, green streptococcus, hemolytic streptococcus	No growth
C. B. 2 yr.	Bronchopneumonia, acute bronchitis, acute laryngitis, acute tracheitis	Throat: Klebs-Loeffler bacillus negative, 10 per cent hemolytic streptococcus, green streptococcus predominating	Klebs-Loeffler bacillus negative (no plate cultures)	Green streptococcus, Staphylococcus albus, hemolytic streptococcus	Hemolytic streptococcus
H. W. 19 mo.	Confluent bronchopneumonia, acute tracheitis, acute bronchitis	Throat: Klebs-Loeffler bacillus negative, 40 per cent hemolytic streptococcus, 50 per cent green streptococcus	Klebs-Loeffler bacillus negative, hemolytic streptococcus, green streptococcus	Hemolytic streptococcus	Not cultured

from cases of laryngitis were injected intraperitoneally into mice. They were nonpathogenic in doses up to 0.5 cc. of a twenty-four hour broth culture.

In only one case in this series could tetany be a possible factor; in all the others, routine chemical analysis of the blood revealed a normal calcium and phosphorus content. Enlarged thymus and other causes of laryngeal obstruction were eliminated.

The clinical history, the low percentage of hemolytic streptococci in the laryngeal flora and the observations on direct laryngoscopic examination suggest that this group of cases may represent severe types of so-called acute catarrhal laryngitis. Perhaps a more suitable term for the condition is "acute laryngotracheobronchitis," as suggested by Baum.

SUMMARY AND CONCLUSION

A comparative clinical study of a group of thirty-eight children with laryngeal diphtheria with a group of twenty-eight cases of nondiphtheritic laryngitis is presented.

In general the clinical observations are very similar in the two groups, all patients showing symptoms and signs of obstructive laryngitis.

Of clinical importance in the diphtheritic group is the fact that on careful inspection a membrane could be seen in the throat of thirty-one of the thirty-seven patients. The initial culture was positive for *B. diphtheriae* in thirty-seven of the thirty-eight cases, and in the one exception a tube culture was positive.

In the nondiphtheritic group, a definite membrane was not present in any of the patients' throats when either direct or laryngoscopic examination was made. Several showed excessive amounts of mucus and loose exudate. In all of these cases cultures for *B. diphtheriae* were negative, and the percentage of hemolytic streptococci was low. This evidence in the study of this group of cases strongly suggests that they were severe types of acute catarrhal laryngitis rather than hemolytic streptococcic infections.

In this group of cases the predominating organism found by poured blood-agar plate cultures from the larynx was a green-producing streptococcus. Hemolytic streptococci were insignificant in this series of cases. Organisms of lesser frequency were *Pneumococcus type* IV; *Micrococcus catarrhalis, Staphylococcus aureus; Staphylococcus albus* and *B. influenzae*.

From the bacteriologic study of this group of cases, it is suggested that green-producing cocci may be of etiologic significance in certain types of acute obstructive laryngitis simulating laryngeal diphtheria.

THE NUTRITION OF SICK CHILDREN*

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AND
IRMA HUG, Sc.B.
MILWAUKEE

The purpose of this investigation was to determine the food requirements of children with chronic diseases, particularly those having tuberculous bone lesions. Observations were also made of the appetite, choice of foods selected, the influence of vitamin B and the effect of supplementary foods, especially of malted milk prepared in various forms. No similar study has been found in the literature. McCann and Barr[1] reviewed the investigations concerning the dietary of tuberculous patients and reported a study of fourteen tuberculous adults. The basal metabolism was approximately normal. Small increases of metabolism occurred with rises of body temperature. The food requirements of adult tuberculous patients were not large.

Thirteen children were studied. Table 1 gives the initials of the thirteen children, the age, sex, height, "normal" average height, weight, "normal" average weight, percentage over or under "normal weight," surface area and activity. Table 2 gives the diagnoses, state of nutrition and appetite of the patients at the beginning of the period, the clinical progress and the weight response. The patients ranged in age from 2 years and 11 months to 12 years and 7 months. There were ten boys and three girls. Nine patients had tuberculous bone lesions, two, chronic, nontuberculous osteomyelitis and two, healing fractures. Four patients, M. B., R. S., C. K. and V. G., were up and about most of the day but were confined to their rooms. All the other patients were kept in bed in the orthopedic ward. They were exposed on the hospital roof to the sky or sun whenever the weather permitted.

A complete physical examination of each patient was made at the beginning of the period and at monthly periods throughout. The patients were seen daily, and the usual hospital charts were kept. The

* Submitted for publication, Feb. 21, 1930.

* From the Department of Pediatrics, Marquette University Medical School, and the Milwaukee Children's Hospital.

* This investigation was made possible by a grant from Mr. Horlick of the Horlick Malted Milk Company of Racine.

1. McCann, W. S., and Barr, D. P.: Clinical Colorimetry: Metabolism in Tuberculosis, Arch. Int. Med. **26**:663 (Dec.) 1920.

TABLE 1.—*Body Measurements, Weight and Activity of Patients*

Name	Sex	Age at Start Yr.	Age at Start Mo.	Height at Start In.	Height at Start Cm.	Average Height* in Inches	Weight at Start Lbs.	Weight at Start Kg.	"Normal" Average Weight for Age and Actual Height* Lbs.	"Normal" Average Weight for Age and Actual Height* Kg.	Percentage* Under or Over-weight	Surface Area,† Sq. Meters	Activity
R. M.	M	12	..	52¾ L.	131.9	58	51	23.1	68	30.9	—25	0.94	In bed, flat on back
C. K.	M	10	7	52⅛	131.3	56	55	25.0	67	30.4	—18	0.98	Up and about in room
L. S.	M	10	5	54 L.	135.0	56	58 Apr. 18	26.3	70	31.8	—17	1.01	In bed, flat on back
J. N.	F	9	10	51 L.	127.5	54	50	22.7	61	27.7	—18	0.91	In bed, flat on back until Aug. 1; then up and about in ward
M. B.	M	9	5	51	127.5	54	68	30.9	61	27.7	+11	1.05	Up and about in room
F. G.	M	9	1	47	117.5	52	51	23.1	50	22.7	+ 2	0.86	In bed, sitting up
R. S.	M	8	5	49½	123.8	49	50½	22.9	58	26.3	—13	0.89	Up and about in room
B. K.	M	7	11	45 L.	112.5	49	39¼	17.8	46	20.9	—15	0.75	In bed, flat on back
S. L.	F	6	9	42 L.	105.0	47	37¼	16.9	39	17.7	— 4	0.70	In bed, flat on back
G. C.	M	6	1	43	107.5	44	36¼	16.4	41	18.6	—12	0.71	In bed, sitting up; walking
W. S.	M	3	7	39 L.	97.5	40	34 May 30	15.4	35	15.9	— 3	0.57	In bed, flat on back
A. J.	F	3	8	35 L.	87.5	39	25½ Feb. 21	11.5	29	13.1	—12	0.50	In bed, flat on back
G. K.	M	2	8	34 L.	85.0	37	25½ Jan. 31	11.5	27	12.2	— 6	0.50	In bed, flat on back

L = length.
* Calculated from the Baldwin Wood height-weight age tables.
† Calculated from the Du Bois height-weight formula.

TABLE 2.—*The Diagnoses, Nutritive and Clinical Progress of the Patients*

Initials	Diagnosis	State of Nutrition	Appetite at Start	Clinical Progress	Weight at End
R. M.	Tuberculosis old, both knees and left hip; chest clear	Poor	Poor	Very little	Very slight gain
C. K.	Healed osteomyelitis left tibia; chronic osteomyelitis with sinus left humerus	Fair	Good	Good	Excellent gain
L. S.	Tuberculosis of right hip; chest clear	Fair	Good	Fair	Slight gain
J. N.	Tuberculosis lumbar spine; chest clear	Poor	Good	Very little	Slight gain
M. B.	Chronic osteomyelitis right tibia; chest clear	Excellent	Good	Good	Excellent gain
F. G.	Osteomyelitis left lower femur and right humerus; chest clear	Fair	Fair	Very little	Very little gain
R. S.	Healing fracture left tibia, fibula; chest clear	Fair	Fair	Good	Good gain
B. K.	Tuberculosis fifth to eighth thoracic vertebrae and right knee	Poor	Poor	Very little	Loss
S. L.	Tuberculosis left hip; infected tonsils	Fair	Fair	Very little	Slight gain
G. C.	Tuberculosis right hip; chest clear	Fairly good	Fair	Fair	Good gain
W. S.	Tuberculosis of left hip	Good	Poor	Fair	Very slight gain
A. J.	Tuberculosis eighth to twelfth thoracic vertebrae	Poor	Poor	Very little	Slight gain
G. K.	Tuberculosis ninth and tenth thoracic vertebrae; marked anemia; glands of hilus enlarged	Poor	Fair	None	Very little gain

Wassermann and microprecipitation tests were negative in all cases. The erythrocyte count, hemoglobin, leukocyte count and differential blood count were made at the beginning and at monthly intervals throughout (table 3). A complete urinalysis was made at the beginning and at weekly intervals on each patient. Four patients, S. L., B. K., A. J. and G. K., presented abnormalities in the urine.

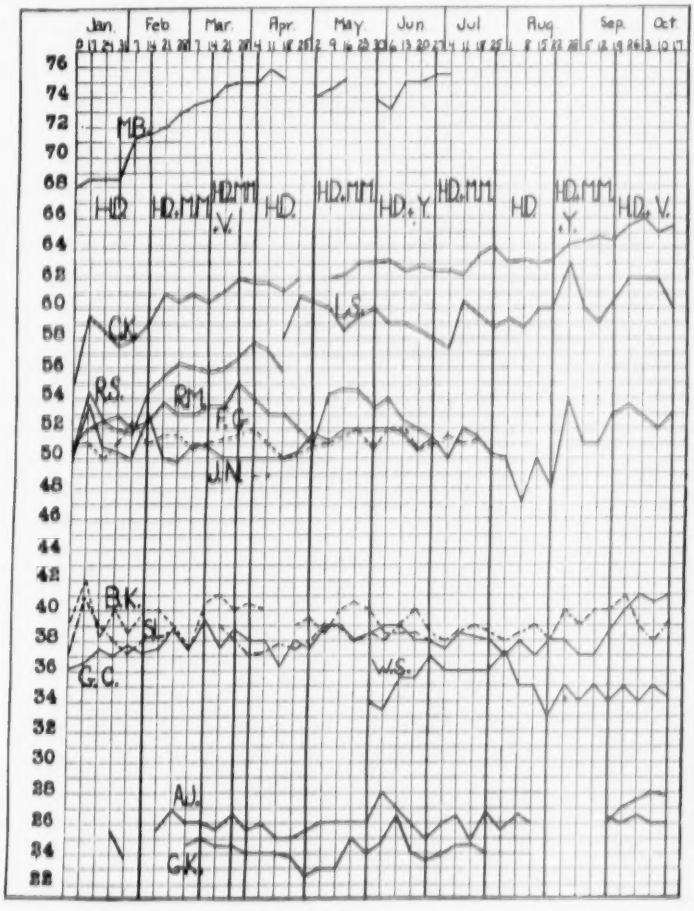

Chart 1.—Weight curves of all of the patients during the entire period of observation. In this and the succeeding charts, *H.D.* indicates house diet; *M.M.*, malted milk; *V*, Vivatose, and *Y*, compressed yeast. The appetite was recorded as poor, fair or good.

Any unusual developments in the physical condition of the patients during the period of study were noted. The patients were weighed at the outset and once a week thereafter. Standing and sitting heights were obtained once a month except for the bed patients; the body length

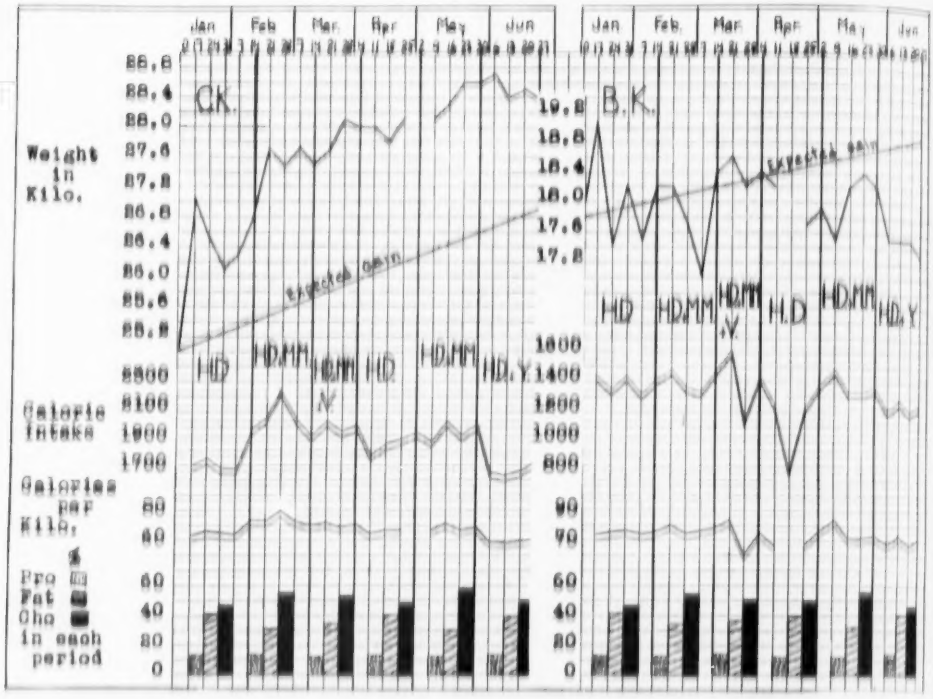

Chart 2.—Curves showing the two extremes in response: one a rapid gain, the other a loss over the period of observation. In this and the succeeding charts the expected gain was according to Holt and Howland: Diseases of Infancy and Childhood, New York, D. Appleton & Company, 1927, p. 17.

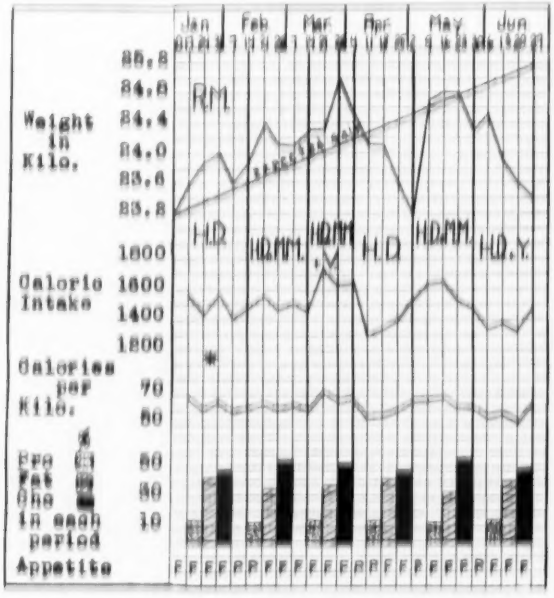

Chart 3.—Curves for R. M. On January 28, pus was aspirated from the right knee.

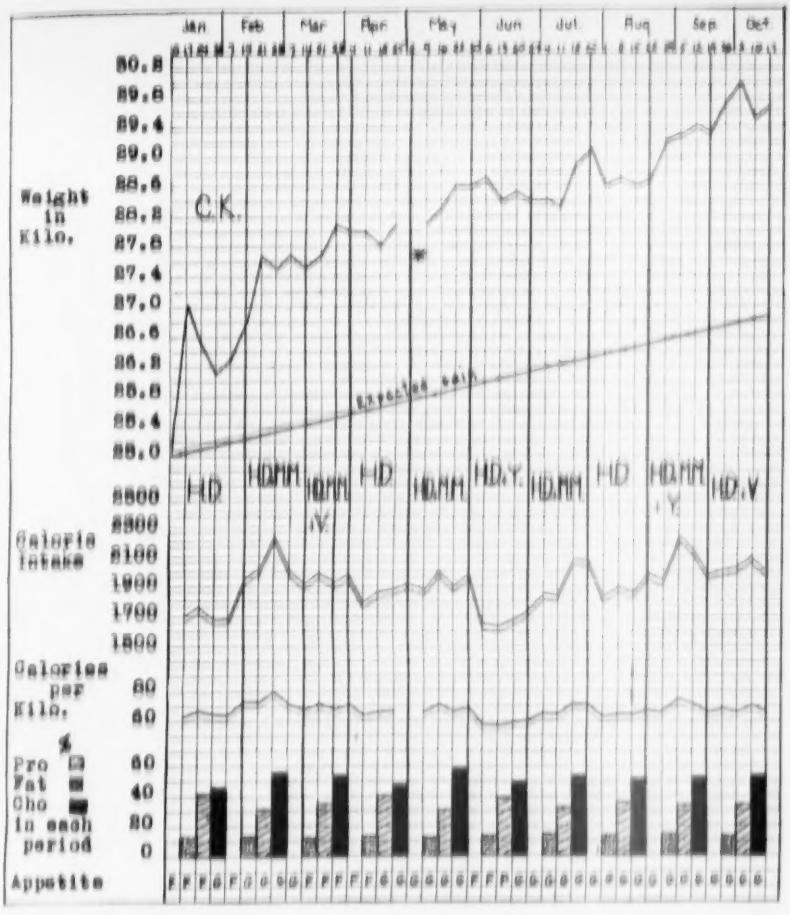

Chart 4.—Curves for C. K. On May 2, the patient was isolated for observation.

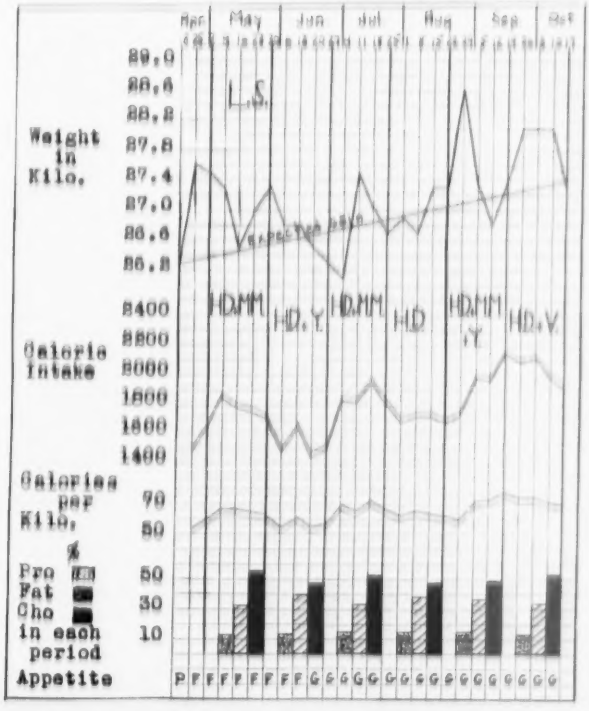

Chart 5.—Curves for L. S.

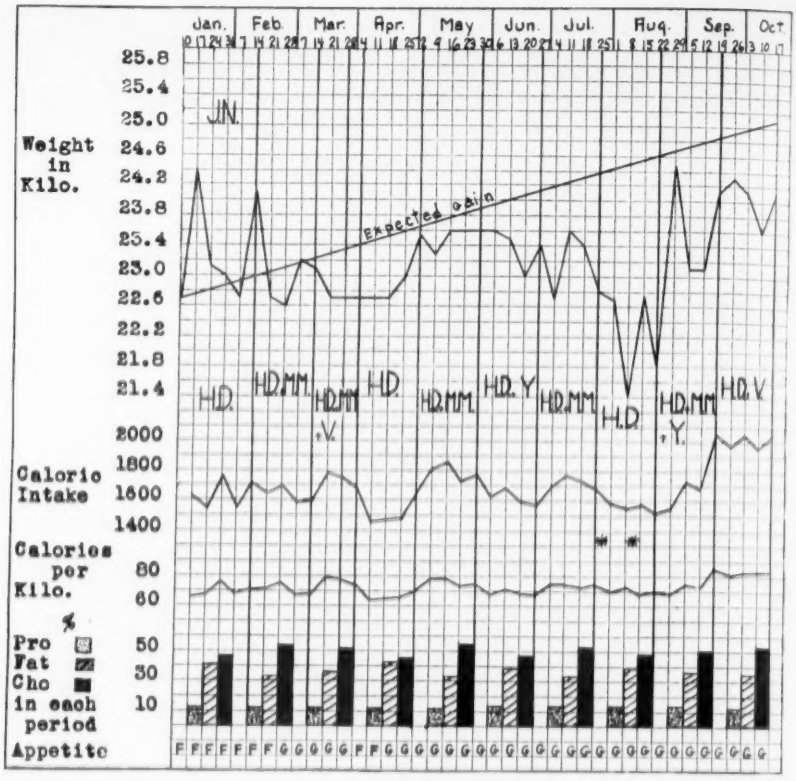

Chart 6.—Curves for J. N. On July 27 and 29, pertussis vaccine was administered; on August 14, the patient was up and walking.

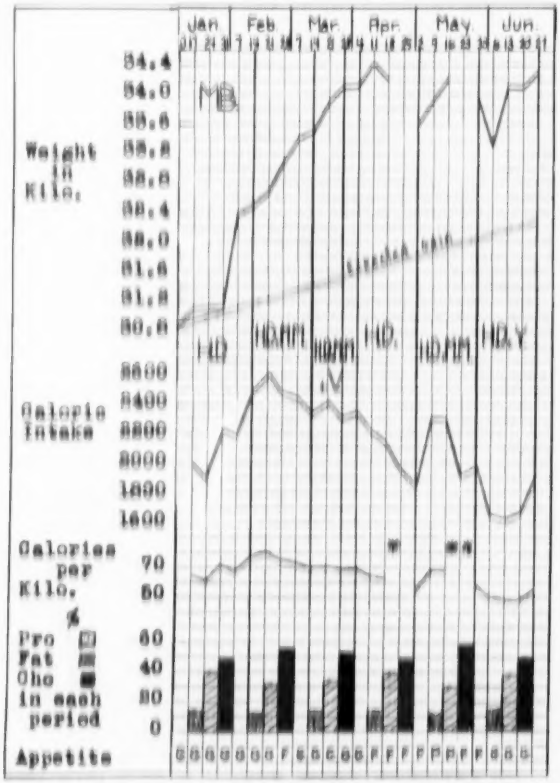

Chart 7.—Curves for M. B. On April 24, sequestra were removed; on May 17, erysipelas was noted; on May 19, the patient was transferred to the isolation ward, and on May 28, he was transferred back.

TABLE 3.—*Blood Counts, Abnormal Urinary Observations and Special Tests*

Initials	Date	Hemoglobin	Red Blood Cells	White Blood Cells	Small Lymphocytes	Large Lymphocytes	Large Mononuclears	Neutrophils	Transitionals	Eosinophils	Basophils
R. M.*	1/16	68	499	5,400	40.5	1	...	57	...	1.5	...
	1/30	65	463	6,800	28	10.5	1	56	1.5	2	1
	3/ 4	65	431	8,200	37	5	2	55	...	...	1
	4/ 3	60	327	7,400	23	7	6	61	...	3	...
	5/ 3	63	664	5,800	41	6	2	50	...	...	1
C. K.	1/17	66	443	11,000	25	6.5	2.5	66	...	...	...
	3/ 4	76	444	12,500	45	4.5	1.5	49	...	...	...
	4/ 4	60	485	11,200	36	6	...	58	...	...	...
	5/24	58	458	12,200	30	5.5	0.5	63	...	1	...
	6/12	53	424	10,600	27	5.5	3	63	1	0.5	...
	9/ 4	65	384	8,600	8.5	37.5	5	48	1	...	...
L. S.	4/15	60	3.89	10,000	31	2.5	1.5	64	1	...	...
	5/ 3	66	4.41	7,600	35	15.0	2	46	1	1	...
	7/ 2	70	4.11	6,000	21	10	5	63	...	1	...
	8/ 5	58	4.44	8,400	32	8.0	6	54	...	...	...
	9/ 4	58	4.15	8,400	21	11	2.5	64.5	0.5	0.5	...
	10/ 9	72	3.72	5,800	36	10.5	2	50.5	...	1	...
J. N.	1/16	47	4.30	9,000	32	....	2	65	1	...	...
	1/30	52	4.23	7,000	24	5	...	71	...	2	...
	3/ 4	60	3.52	9,000	38	7	3	51	...	1	...
	4/ 3	38	3.91	7,600	18	4	2.5	75	0.5	...	...
	5/ 3	42	4.40	6,400	26	2	1	70	...	1	...
	7/ 2	40	4.50	6,400	20	8	6	64	2	...	...
	8/ 5	45	4.10	6,800	27	10	6	51	...	...	...
	9/ 4	38	3.89	4,000	10	10	3.5	70	0.5	...	...
	10/ 9	57	4.16	7,400	7	6	...	83.5	1.5	2	...
M. B.	1/17	65	456	9,950	24	4	4	65	...	3	...
	3/ 4	80	462	7,400	44.5	3	0.5	48	...	4	...
	4/ 4	70	460	8,000	37	6	1	57	...	...	...
	5/ 4	68	...	7,800	31	6	3	60	...	...	...
	6/10	66	360	7,000	30	6	...	60	...	3	...
	9/17	71	444	13,800	6	10	1	74	...	...	...
	6/18	78	488	6,900	39.5	17.5	4	44.5	...	4.5	...
E. G.	1/16	46	430	13,200	30.5	3	...	60	...	4.5	...
	1/30	45	460	10,000	10	10	0.5	68	1	4.5	...
	3/ 4	67	600	10,000	26	11	1	57	1	3	...
	4/ 3	63	439	8,000	40	4	1	54	...	1	...
	5/ 3	62	654	14,800	54.5	6	0.5	33	...	...	1
	7/ 2	40	401	10,400	26	13	4	54	...	...	...
H. S.	1/17	63	481	18,700	31	1	5	60	...	2	1
	3/ 6	84	661	16,000	30.5	4.5	0.5	59.5	...	...	1
	3/ 4	70	440	9,700	52	7	4	31	...	...	6
	4/ 4	63	400	8,000	41	6	1	50	...	...	...
O. S.†	1/16	50	370	11,400	47	3	...	42	...	8	...
	1/30	60	460	13,000	42	4.5	...	50.5	...	...	...
	3/ 4	60	467	16,000	30	5	...	60	1	...	...
	3/11	60	503	13,300	10	3	3	77	...	...	...
	3/30	50	403	8,800	30	5	4	53	1	...	...
	3/28	70	485	8,800	13.5	3	1.5	83	0.5	1.5	...
	4/ 3	65	451	8,200	30.5	0	5	55.5	...	2	...
	6/ 3	54	360	7,250	33	11	3	52	...	1	...

* 1/8, guinea pig and rabbit inoculated; 2/4/28, guinea pig positive for tuberculosis; rabbit, no tuberculosis; 1/29, pus from knee tuberculous, bacilli found.

† Urine: until 4/16, child had + to ++++ albumin, after that, none; red blood cells and white blood cells until April, 1929; phenolsulphonphthalein, 2/10/29, normal; 2/10/29, nonprotein nitrogen, 37.5; urea, 33.0; urea nitrogen, 15.4.

TABLE 3.—*Blood Counts, Abnormal Urinary Observations and Special Tests—Continued*

Initials	Date	Hemoglobin	Red Blood Cells	White Blood Cells	Small Lymphocytes	Large Lymphocytes	Large Mononuclears	Neutrophils	Transitionals	Eosinophils	Basophils
S. L.‡	1/16	60	4.71	9,800	63	...	...	30	...	7	...
	1/30	62	4.12	10,400	42	0.5	...	51	...	0.5	...
	2/ 3	78	4.54	10,000	37	7	1	55	...	...	...
	4/ 3	52	4.39	7,600	41.5	11.5	4	41.5	1.5	...	...
	5/ 3	65	5.07	8,600	50	4	4	40	1	1	...
	7/ 3	70	5.09	6,800	53	12	4	30	1	1	...
	8/ 5	50	4.09	7,800	46	0.5	4	43	1	0.5	...
	9/ 4	50	3.64	8,400	32	30	2	30	0.5	0.5	...
	10/ 9	65	5.38	11,000	36	18.5	3.5	41	2.5	0.5	...
G. C.	1/16	75	5.67	6,600	30	...	0.5	69.5	...	...	...
	1/30	60	5.31	7,400	50	6	3	53	...	...	...
	3/ 4	73	4.30	10,300	46	13	2	38	...	2	...
	4/ 3	63	5.80	5,800	37	10	3	40	...	2	...
	5/ 3	73	5.73	12,600	35	4.5	5.5	65	...	...	...
	7/ 3	78	5.55	7,000	38	16	4	50	2	...	...
	8/ 5	63	4.53	10,400	30	9	3	49	...	...	...
	9/ 4	60	4.68	7,000	22.5	38.5	5	32.5	1.5	...	...
	10/ 9	63	4.30	8,800	44	9.5	2	43	0.5	1	...
W. S.	5/ 1	73	4.32	7,800	36	5	3	55	...	...	1
	7/ 3	73	5.75	5,600	30	10	4	56	...	...	...
	8/ 5	58	5.30	10,400	33	11	4	58	2	1.5	0.5
	9/ 4	63	5.85	6,600	11	33.5	8	45.5	2	...	...
	10/ 9	65	4.79	12,200	40.5	21	1	36	1.5	0.5	0.5
A. J.§	2/19	60	390	9,200	36.5	9	2.5	51.5	0.5	...	...
	3/ 4	62	454	10,500	38	4	1	51	2	4	...
	4/ 3	60	454	5,400	53	7	...	39	...	1	...
	5/ 3	70	460	10,400	37	9	2	52	...	...	...
	7/ 2	76	390	6,600	40	5	2	51	2	...	...
	8/ 5	62	433	11,600	30	14	2	52	...	1.5	0.5
	10/ 9	70	497	11,200	38	16.5	0.5	42.5	...	2.5	...
G. K.#	1/30	48	364	14,400	30.5	3.5	...	66	...	...	...
	3/ 4	56	427	12,200	26.5	4	4	65	...	0.5	...
	4/ 3	50	437	10,000	24.5	3.5	1.5	70.5	...	...	...
	5/ 3	37	431	14,800	27	14.5	3	54	1.5	...	...
	7/ 2	50	393	12,200	30	5	4	61	...	...	...
	8/ 2	..	...	20,200	29	9.5	0.5	60.5	0.5	...	...
	10/ 9	45	445	10,400	17	7.5	2.5	71.5	...	1.5	...

‡ Urine: 5/20, urine sediment, acid-fast bacilli present; 5/24, guinea-pig inoculation urine positive for tuberculosis; 2/2, acid 1,022, albumin 0, sugar 0, twenty pus cells per field; 2/16, acid, albumin 0, sugar 0, thirty pus cells per field; all subsequent specimens of urine show + to +++ albumin with pus cells and red blood cells; 5/13, nonprotein nitrogen, 24.0; urea, 22.0; blood urea nitrogen, 10.3; creatinine, 1.17; 2/17, measles to isolation; 2/1, otitis media.

§ Urine: 7/13, albumin ++, occasional pus cell; 5/4, albumin trace, 21 pus cells per field.

Urine: 2/8, albumin +++, diacetic acid +; 7/6, albumin ++; 7/13, albumin +, occasional red blood cells, 3 pus cells; 7/20, albumin +, 12 pus cells; 8/29, albumin faint trace, occasional pus.

of these was measured monthly. The necessary allowance was made for casts and apparatus.

The study of nutrition was begun Jan. 10, 1929, and continued to Oct. 18, 1929. This time was divided into periods during which various changes were made in the diet. The routine, standard house diet was used for the control and throughout the period as the basic diet. Sample menus for two week periods are illustrative (table 4).

Plain cod liver oil was administered in 10 Gm. doses daily from January to June and 1 ounce of orange juice daily to all patients throughout the experiment. The periods of study were divided as follows: (1) control period of five weeks on basic house diet; (2) four weeks on malted milk dissolved in water, as a beverage substituted for milk; (3) period on malted milk dissolved in water given to supplement

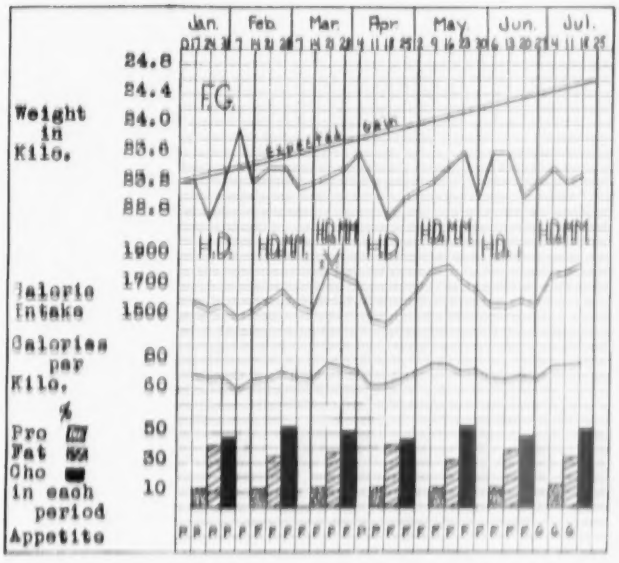

Chart 8.—Curves for F. G.

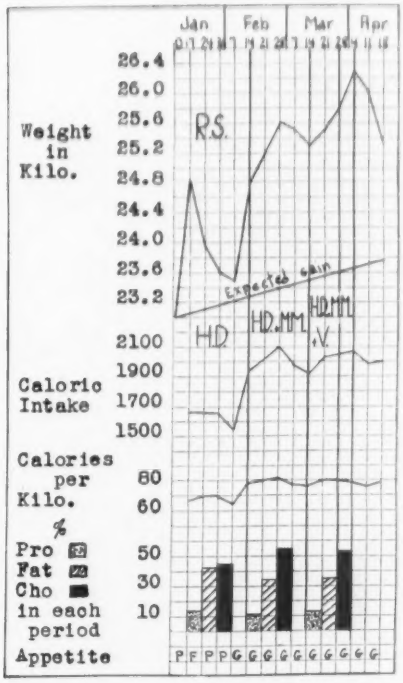

Chart 9.—Curves for R. S.

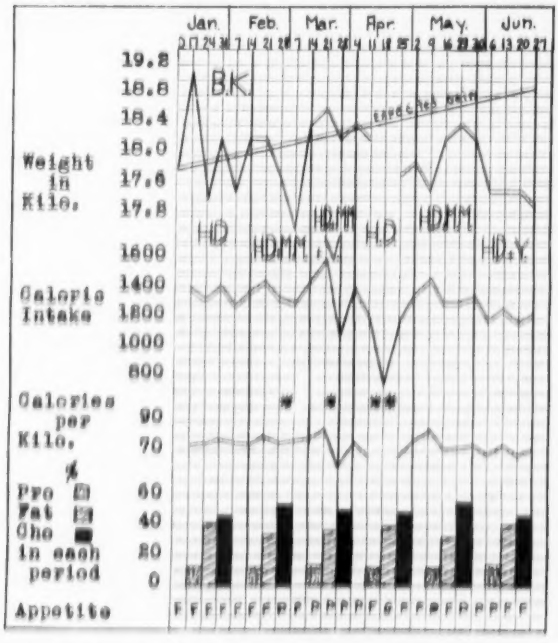

Chart 10.—Curves for B. K. On March 1, cystoscopy was done; on March 26, a transfusion was given; on April 12, stones were removed from the kidney, and the patient was transferred off the floor; on April 22, he was transferred back.

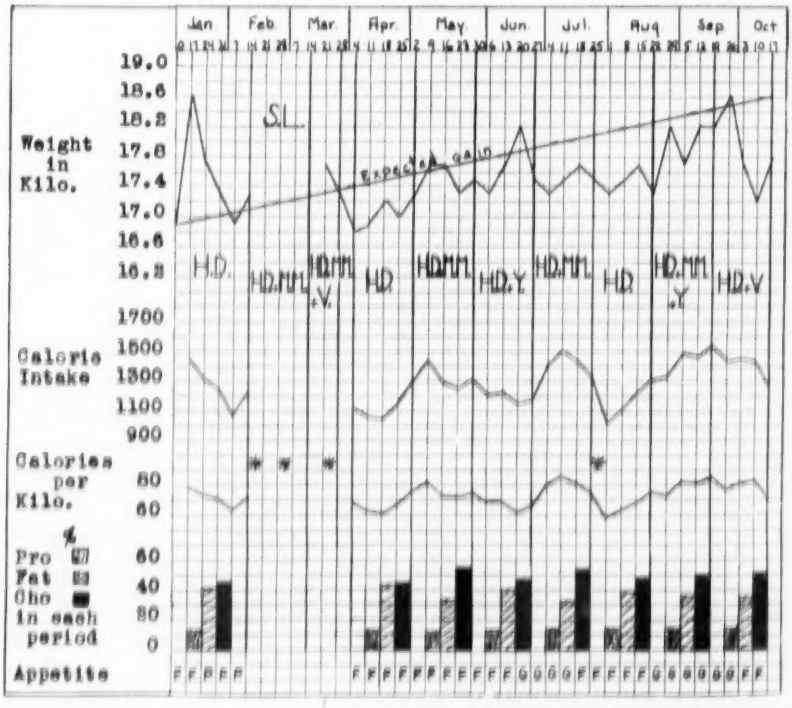

Chart 11.—Curves for S. L. On February 17, the patient had measles and was isolated; on March 1, otitis media was observed and on March 22, pyuria. On March 25, the patient was transferred back, and on July 27 and 29, pertussis vaccine was given.

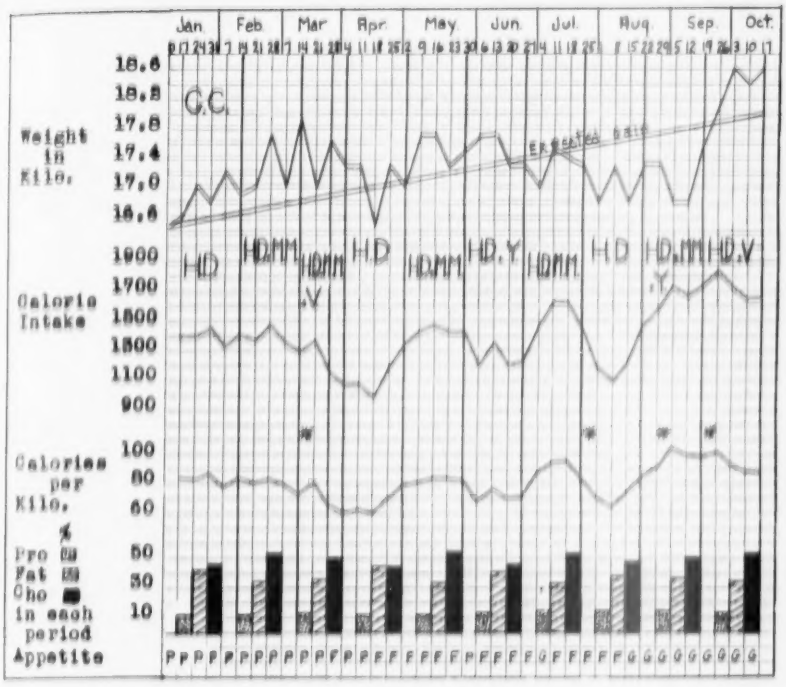

Chart 12.—Curves for G. C. On March 20, the temperature was 102 F.; on March 21, 101 F. On July 27 and 29, pertussis vaccine was administered. On August 30, the patient was sitting up in bed, and on September 23, he was walking with a brace.

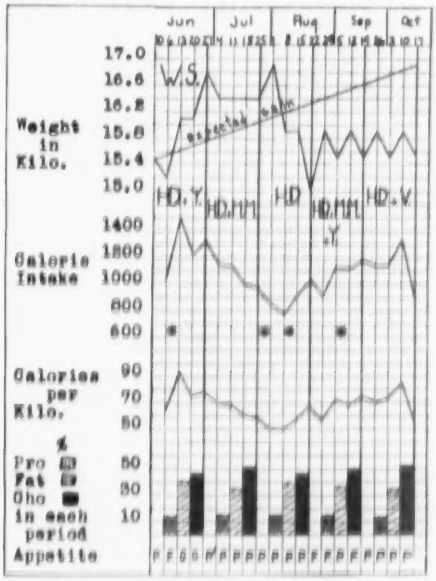

Chart 13.—Curves for W. S. On June 12, a Bradford frame was used; on July 27 and 29, pertussis vaccine was administered. On August 10, the patient was sitting up in bed, on September 10, he was walking and on September 11, he was back on the frame.

TABLE 4.—*Illustrative House Diet Menus Used for the Control and Basic Diets*

Morning	Noon	Evening
Sunday, Feb. 3, 1929		
Orange Cream of wheat Bread Butter Milk	Chicken stew with rice Buttered carrot Fresh tomato Baked custard Bread, butter Milk	Kidney beans Lettuce slaw Peanut butter sandwich Vanilla ice cream Milk
Monday, Feb. 4, 1929		
Prunes Cream of barley Bread, butter Milk	Bacon Mashed potato Jello with peach Bread, butter Milk	Milk toast Lettuce and tomato slaw Graham bread, jelly Baked apple Milk
Tuesday, Feb. 5, 1929		
Applesauce Pettijohn's Bread, butter Milk	Lamb stew Bread, butter Sponge cake Milk	Cornmeal Lettuce slaw Graham toast, honey Peaches Milk
Wednesday, Feb. 6, 1929		
Banana Puffed rice Bread, butter Milk	Liver loaf Mashed potato Tomato with bread Bread, butter Jello Milk	Vegetable soup Soda cracker Cottage cheese Graham bread, peanut butter Apricots Milk
Thursday, Feb. 7, 1929		
Orange Oatmeal Bread, butter Milk	Meat cakes Baked potato String beans Bread, butter Orange pudding Milk	Cream of wheat with dates Lettuce slaw Graham bread, honey Pears Milk
Friday, Feb. 8, 1929		
Prunes Wheatena Bread, butter Milk	Steamed halibut Mashed potato Buttered beets Bread, butter Ice cream Milk	Cream of potato soup Fresh tomato Graham bread, peanut butter Applesauce Milk
Saturday, Feb. 9, 1929		
Orange Wheatena Bread, butter Milk	Scrambled eggs Baked potato Buttered carrot Chocolate pudding Bread, butter Milk	Macaroni with milk and butter Lettuce and tomato slaw Graham bread, peanut butter Peaches Milk
Sunday, Feb. 10, 1929		
Banana Puffed wheat Bread, butter Milk	Roast chicken, gravy Mashed potato Creamed carrot Floating island Bread, butter Milk	Chicken broth with rice Soda cracker Cole slaw Graham bread, jelly Chocolate ice cream Milk
Monday, Feb. 11, 1929		
Apricots Cream of wheat Bread, butter Milk	Creamed turkey on toast Baked potato String beans Orange Bavarian Bread, butter Milk	Kidney beans Celery Graham bread, jelly Peaches Milk
Tuesday, Feb. 12, 1929		
Applesauce Oatmeal Bread, butter Milk	Lamb chops Mashed potato Spinach Prune whip Bread, butter Milk	Milk toast Lettuce slaw Graham bread, jelly Banana Pennuche candy Milk

TABLE 4.—*Continued*

Morning	Noon	Evening
	Wednesday, Feb. 13, 1929	
Orange Pettijohn's Bread, butter Milk	Bacon Baked potato Buttered carrot Sponge cake Bread, butter Milk	Tomato soup with spaghetti Soda cracker Cabbage slaw Graham bread, jelly Pears Milk
	Thursday, Feb. 14, 1929	
Applesauce Wheatena Bread, butter Malted milk	Meat loaf Buttered peas Mashed potato Baked custard Bread, butter Malted milk	Oatmeal Celery Graham bread, jelly Jello, peaches Malted milk
	Friday, Feb. 15, 1929	
Prunes Cream of wheat Bread, butter Malted milk	Eggs Baked potato String beans Ice cream Bread, butter Malted milk	Vegetable soup Soda cracker Cottage cheese Graham bread, peanut butter Pears Malted milk
	Saturday, Feb. 16, 1929	
Orange Oatmeal Bread, butter Malted milk	Meat loaf Mashed potato Tomato with bread Chocolate pudding Bread, butter Malted milk	Noodles, milk, butter Lettuce and tomato Graham bread, jelly Pineapple Malted milk

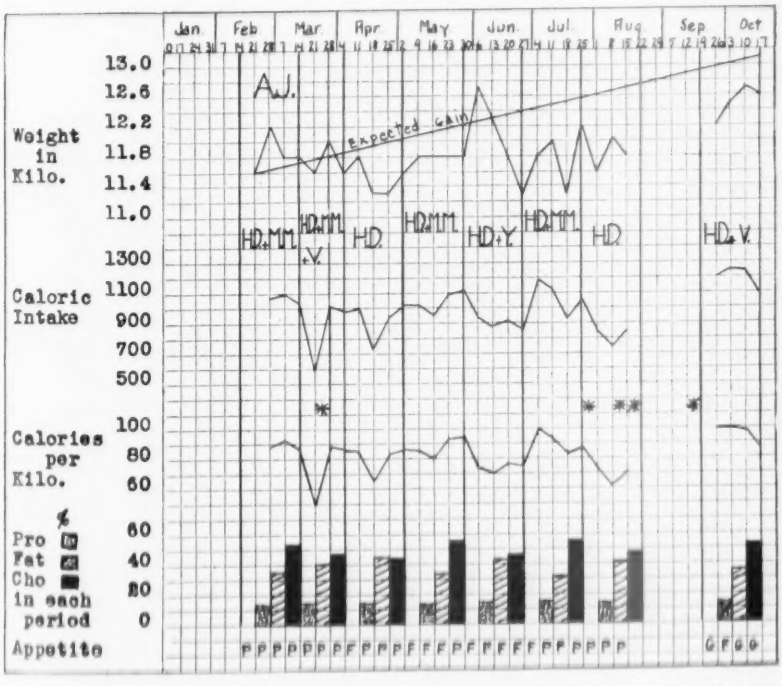

Chart 14.—Curves for A. J. On March 21, the patient was put on a Bradford frame; on July 27 and 29 and on August 10, pertussis vaccine was administered. On August 18, the patient was isolated, and on September 15, she was transferred back.

the basic diet in addition to whole milk as the beverage; (4) period on 12 Gm. of vitamin B supplied in Vitavose daily in whole milk for two weeks; (5) control period of four weeks; (6) period on malted milk dissolved in water concentrated as a beverage in place of whole milk for four weeks; (7) 14 Gm. of yeast added daily to the basic diet for four weeks; (8) period on malted milk dissolved in milk as a beverage; (9) control period on basic diet; (10) period on 14 Gm. of yeast daily;

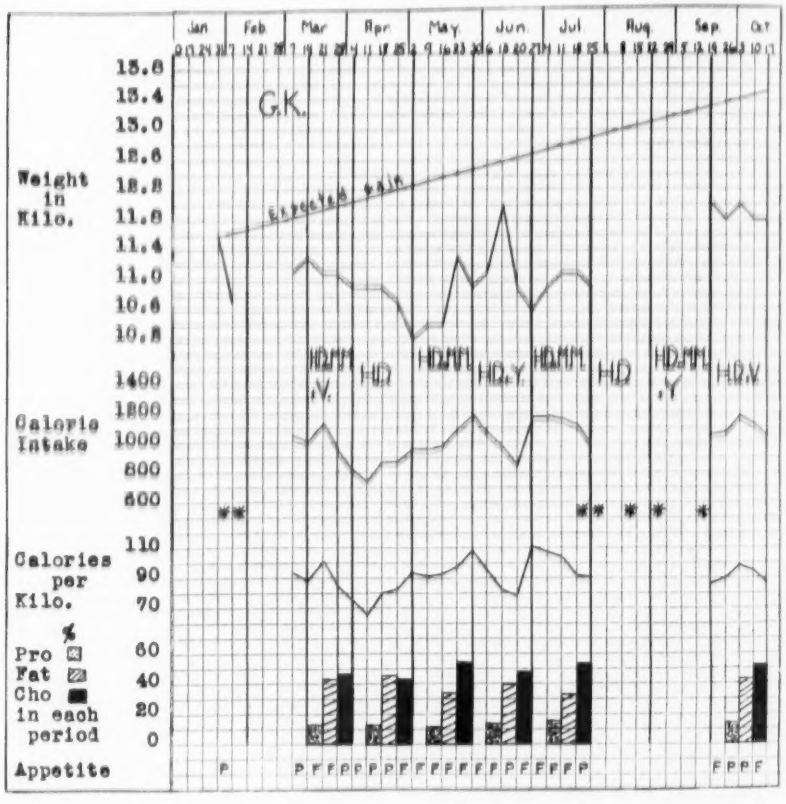

Chart 15.—Curves for G. K. On February 2, three teeth were extracted; on February 8, the patient had measles and was isolated on the following day. On July 22, 24, 27, 29 and 31, pertussis vaccine was administered. On July 26, the patient was isolated and pertussis vaccine was given; on August 10, he was transferred back. On August 26, he was again isolated, and on September 15, he was transferred back.

malted milk if, and as, desired in addition to whole milk as a beverage, and (11) period on basic diet plus Vitavose, 36 Gm. daily (table 5).

During the entire period all food was weighed and measured. It was served on individual trays to the children at their beds. They were allowed to eat as much food as they desired, but a balanced ration was

suggested. Second and third helpings were usually available. The carbohydrate, protein and fat content of all food eaten was calculated, and the total calories computed.

Chart 1 illustrates the weight curves of all of the patients during the entire period. The changes in diet are indicated. Chart 2 indicates the two extremes in response, one a rapid gain, the other a loss over the period. Charts 3 to 15 illustrate the individual responses to the diet.

TABLE 5.—*The Periods of Study, Showing the Composition of Each Supplementary Food*

		Daily Supplementary Food	Weight	Protein	Fat	Carbohydrate	Calories
Jan. 10–Feb. 14	Basic house diet (control period) 5 weeks	Whole milk 3 servings	426	14.07	17.04	21.30	294.9
Feb. 14–Mar. 14	HMM in water used as beverage (no whole milk) 4 weeks	HMM* and water 3 servings	420	12.00	0.48	50.10	260.9
Mar. 14–Apr. 4	HMM in water given to supplement whole milk 1 qt. 3 weeks	HMM and water 3 servings	426	10.08	5.70	44.43	271.5
Mar. 16–Mar. 29	18 Gm. "Vitavose" given daily in whole milk 2 weeks	"Vitavose"†	18	1.80	....	9.90	44.4
Apr. 4–May 2	Basic house diet, whole milk as only beverage (control period) 4 weeks	Whole milk 3 servings	426	14.07	17.04	21.30	294.9
May 2–May 30	HMM in water as only beverage in concentrated form, 4 weeks	HMM and water 3 servings	420	30.61	11.10	85.80	525.6
May 30–June 27	Basic house diet with one cake compressed yeast daily, 4 weeks	Yeast‡	14	1.64	0.06	2.94	18.8
June 27–July 25	HMM in milk as only beverage, 4 weeks	HMM and milk 3 servings	420	21.42	19.65	58.80	497.7
July 25–Aug. 22	Whole milk as only beverage (control period) 4 weeks	Whole milk 3 servings	426	14.07	17.04	21.30	294.9
Aug. 22–Sept. 19	Basic house diet with one cake compressed yeast daily, and HMM in water as and if desired, 4 weeks	HMM and water 3 servings Yeast	420 14	29.82 1.64	22.68 0.06	99.12 2.94	720.0 18.8
Sept. 19–Oct. 17	Basic house diet with 36 Gm. "Vitavose" daily 4 weeks	"Vitavose"	36	5.40	....	28.08	130.92

* Horlick's malted milk.
† "Vitavose" commercial preparation, E. R. Squibb & Co.
‡ Compressed yeast, Red Star Yeast Company.

COMMENT

An examination of table 1 reveals that at the beginning of the study only two patients were over average weight, one 2 per cent. All of the others were from 3 to 25 per cent under average weight. One patient was one-half inch (1.27 cm.) above average height; the others were from 1 inch to 5¼ inches (2.54 to 13.97 cm.) below average height. It must be pointed out that four of these had tuberculous disease of the spine. These children form the typical group usually found in the

orthopedic wards of any children's hospital. In the charts it will be noted that only four patients (three nontuberculous) made expected gains in weight, M. B., C. K., R. S. and G. C. The first two had chronic osteomyelitis; the third, a healing fracture, and the fourth, tuberculosis of the right hip. The clinical progress of the first three patients was satisfactory.

All of these children were given excellent orthopedic and medical attention. It had been assumed that the diet was adequate. Four of the children had poor appetites, five had fair and four had good appetites. All but four were considered to have been provided with suffi-

TABLE 6.—*Average and Actual Basal Requirement Based on Surface Area, and Actual Average Caloric Intake for One Day*

Name	Age January 1929 Yr.	Mo.	Sex	Average Surface Area in Sq. Meters*	Average Basal Requirement Based on Surface Area†	Actual Basal Requirement Based on Surface Area	Actual Average Total Caloric Intake for One Day	Percentage of Actual Intake Above Basal Requirement	Gain + or Loss — Pounds	Period of Observation, Weeks
R. M.	12	..	M	1.15	1,325	1,083	1,490	38	+ ½	25
C. K.	10	7	M	1.11	1,305	1,152	1,910	66	+ 10½	40
L. S.	10	5	M	1.13	1,350	1,212	1,789	48	+ 2	26
J. N.	9	10	F	1.03	1,169	1,030	1,689	65	+ 3	40
M. B.	9	5	M	1.03	1,201	1,260	2,130	69	+ 7½	25
F. G.	9	1	M	0.93	1,158	1,053	1,647	56	+ ¼	27
R. S.	8	5	M	0.95	1,180	1,111	1,898	71	+ 5¼	14
B. K.	7	11	M	0.86	1,103	959	1,360	38	— 1¼	25
S. L.	6	9	F	0.77	924	840	1,290	54	+ 2	34
G. C.	6	1	M	0.73	946	939	1,400	53	+ 4¾	40
W. S.	3	7	M	0.60	887	766	1,086	42	+ ¼	20
A. J.	3	8	F	0.58	758	636	995	56	+ 2¼	30
G. K.	2	8	M	0.56	766	684	1,006	47	+ ½	27

* Calculated from the Du Bois height-weight formula.
† Calculated from the Baldwin-Wood weight-height-age tables.

cient food. An analysis of tables 6 and 7, however, reveals that the nutritional provision was not adequate. The caloric intake ranged from 38 to 71 per cent above the calculated basal food requirement based on actual weight. On the basis of a normal weight based on normal height for age, the intake ranged from 9 to 69 per cent above the basal requirement. Only those patients made satisfactory gains in weight who received 46 per cent or more calories above the basal requirement based on their "normal" surface area. Other factors, such as activity and extent of the disease process and physical activity, enter into the problem. It is surprising to note that children encouraged to eat and given supplementary food, who appear to be getting adequate food, may actually receive from 9 to 69 per cent above the optimum basal require-

ment for the expected weight. These nongaining children require special attention and concentrated foods, as suggested by Nobel, Pirquet and Wagner[2] and Hord and Roberts.[3]

Six children gained consistently whenever they received malted milk, especially when this food was served dissolved in water as the only beverage. This food is known to contain vitamins A, B_1 and B_2.[4]

TABLE 7.—*Summary of Data, Showing the Actual Average Calories Per Kilogram of Body Weight Taken, and the Relation Between This and the Actual and Average Basal Requirement*

Name	Age Yr.	Age Mo.	Average Basal Requirement* in Calories per Kg., Based on First Wt.	Average Basal Requirement* in Calories per Kg., Based on Last Wt.	Actual Basal Requirement† in Calories per Kg., Based on First Wt.	Actual Basal Requirement† in Calories per Kg., Based on Last Wt.	Actual Average Caloric Intake per Kg., Based on First Wt.	Actual Average Caloric Intake per Kg., Based on Last Wt.	Percentage of Actual Intake Above Actual Basal Requirement	Ratio Between Actual Basal Requirement and Caloric Intake	Percentage of Actual Intake Above Normal Basal Requirement	Gain for Entire Period in Kg.	Activity
R. M.	12	..	57	56	47	46	64	64	38	1.38	12	0.23	In bed, on back
C. K.	10	7	52	44	46	39	76	64	66	1.65	46	4.77	Up and about in room
L. S.	10	5	52	49	46	44	68	66	48	1.48	32	0.91	In bed, on back
J. N.	9	10	51	48	45	43	75	70	64	1.64	46	1.36	In bed, on back to Aug. 4; then up in ward
M. B.	9	5	41	37	41	37	78	69	69	1.69	69	3.41	Up and about in room
F. G.	9	1	49	49	45	45	71	71	56	1.56	45	0.11	In bed, sitting up
H. S.	8	5	51	47	48	44	82	75	71	1.70	60	2.39	Up and about in room
B. K.	7	11	67	69	53	54	72	75	39	1.39	9	—0.57 loss	In bed, on back
S. L.	6	9	55	52	50	47	82	72	54	1.53	40	0.91	In bed, on back
G. C.	6	1	57	51	58	49	85	76	53	1.52	49	2.46	In bed, on back and sitting up
A. J.	3	8	64	59	55	50	86	79	56	1.56	35	1.02	In bed, on back
W. S.	3	7	57	57	49	49	70	70	42	1.41	22	0.11	In bed, on back
G. K.	2	8	66	65	50	58	87	85	47	1.47	31	0.23	In bed, on back

* Du Bois height-weight formula for actual age of child, but with normal weight and height.

† Du Bois height-weight formula using patients' age, weight and height.

Commercial yeast and Vitavose had no apparent effect on the appetites of these children.

There was a remarkable constancy in the composition of foods self-selected. Additional helpings of any food were usually available to the children. The protein intake averaged between 12 and 14 per

2. Nobel, E.; Pirquet, C., and Wagner, R.: The Nutrition of Healthy and Sick Infants and Children, English translation, Gasul, Philadelphia, F. A. Davis Company, 1929.

3. Hord, N., and Roberts, L. J.: J. Am. Diet. A. **4**:77 (Sept.) 1928.

4. Quinn, E. J., and Brabec, L. B.: J. Home Economics **22**:123 (Feb.) 1930.

cent, the carbohydrate between 49 and 52 per cent, and the fat between 35 and 38 per cent of the total calories (table 8).

The only consistent feature of the individual charts is the rough parallel between the clinical condition and the weight curve of the patient. The three patients who made good progress clinically gained steadily in weight unless an interruption occurred, such as an operation or an infection.

The eight patients who made slight gains reflect in their weight charts their clinical progress. Three of the four nontuberculous patients made good clinical progress and expected gains in weight.

TABLE 8.—*Average Daily Food Intake in Grams and Percentage of Total Calories for Entire Time*

	Carbohydrate, Gm.	Per Cent	Protein, Gm.	Per Cent	Fat, Gm.	Per Cent	Calories
R. M.	189	50	47	13	61	37	1,490
C. K.	240	52	63	13	74	35	1,910
L. S.	230	51	60	13	70	36	1,780
J. N.	214	50	56	13	68	37	1,692
M. B.	278	52	68	13	83	35	2,190
F. G.	205	50	51	13	67	37	1,647
R. S.	244	51	68	13	77	37	1,898
B. K.	164	51	39	12	54	37	1,390
S. L.	160	50	40	13	53	37	1,390
G. C.	175	50	46	13	58	37	1,490
W. S.	134	49	36	14	45	37	1,086
A. J.	125	49	32	13	41	38	995
G. K.	125	50	32	13	42	37	1,006

CONCLUSIONS

The food requirements of children with chronic bone disease, especially tuberculous disease, are not high but should exceed 50 per cent above the basal requirements calculated on the basis of the "normal" or expected average weight and the height. For patients from 2 to 6 years of age, more than 90 calories per kilogram of body weight should be given; for those from 6 to 12 years, more than 80 calories per kilogram are necessary. These requirements are approximately those for normal, well, active children, but they must be supplied to the sick children in bed.

The effects of concentrated foods and further modifications of the diet are being studied.

Dental caries did not develop in any child.

NORMAL CLOSING TIME OF THE FORAMEN OVALE AND THE DUCTUS ARTERIOSUS

AN ANATOMIC AND STATISTICAL STUDY*

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NEW YORK

Statements regarding the closing time of the foramen ovale and the ductus arteriosus vary markedly in the literature. Therefore it seemed worth while to study the material available from necropsies performed at the Babies' Hospital in order to determine more accurately when these fetal openings are closed after birth.

In Gray's "Anatomy"[1] it was stated that the foramen ovale is closed ten days and the ductus arteriosus in from four to ten days after birth. Holt and Howland[2] (1928) said that the closing time of the foramen is the middle of the first year, and that the ductus is invariably obliterated in twenty days. Griffith and Mitchell[3] gave the closing time of the foramen as several months after birth or during the second year, and that of the ductus as one or two weeks after birth. Patten and Taggart's[4] recent article contains the statement that the foramen is closed late in the last half of the first year. Arey[5] found the ductus closed within three months; only one third of his patients, however, showed a closed foramen in three months, and in three quarters it was closed by maturity. Abbott[6] said that the ductus arteriosus is closed in the third week of life. She gave no specific time for the closing of the foramen ovale, but remarked that its lack of closure is not pathologic. Dragendorff[7] quoted Hinze[8] as believing it practical to assume that complete

* Submitted for publication, Feb. 27, 1930.

* From the Pathological Department of the Babies' Hospital and the Pediatric Department of Columbia University College of Physicians and Surgeons.

1. Gray, Henry: Anatomy, ed. 20, Philadelphia, Lea & Febiger, 1918, p. 542.

2. Holt, L. E., and Howland, John: Diseases of Infancy and Childhood, ed. 9, New York, D. Appleton & Company, 1926, p. 452.

3. Griffith and Mitchell: The Diseases of Infants and Children, Philadelphia, W. B. Saunders Company, 1927, vol. 2, p. 377.

4. Patten, B. M., and Taggart, W. B.: An Unusual Type of Triatrial Heart, Arch. Path. **8**:894 (Dec.) 1929.

5. Arey: Developmental Anatomy, Philadelphia, W. B. Saunders Company, 1924, p. 203.

6. Abbott, Maude: Congenital Cardiac Disease, in Osler: System of Modern Medicine, Philadelphia, Lea & Febiger, 1927, vol. 4, p. 612.

7. Dragendorff, O.: Handbuch der Anatomie des Kindes, Munich, J. F. Bergmann, 1920, vol. 2, p. 300.

8. Hinze, Berlin Dissert, 1893, cited by Dragendorff (footnote 7).

closure of the foramen ovale occurs in the second year, although the closing process is especially active during the first two months of life and then becomes slower. He found children 1 year of age with foramina as large as at birth. Alexejeff[9] found the earliest complete closure to be at forty days, and that in the majority of cases complete closure took place in from five to seven months. Patency occurs in as high as 30 per cent of adult hearts, according to Tandler,[9] but in most cases the foramen ovale is represented by only a very small opening.

I reviewed more than 500 consecutive autopsies, excluding all congenitally malformed hearts, and plotted the percentage of open and closed

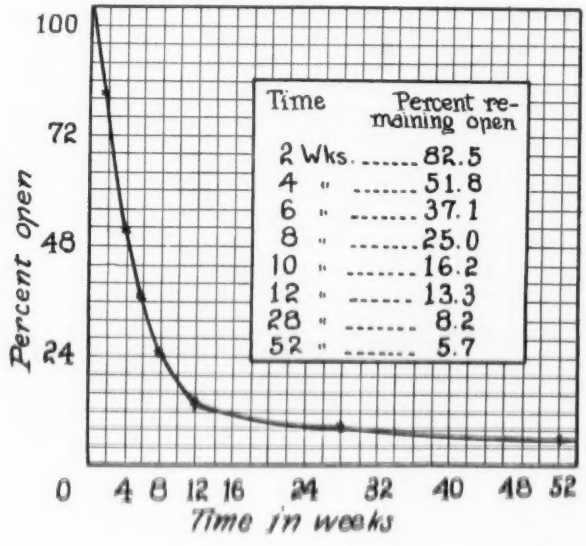

Chart 1.—Normal closing time of the foramen ovale in 500 normal hearts of infants from 1 day to 1 year of age.

fetal openings at different ages calculated in weeks. It is apparent from the accompanying graphs that at some point along their contour the points of optimum or normal closure will be found, while all points after this tend toward the abnormal or pathologic closing time.

The ductus arteriosus was examined in 558 consecutive normal hearts, and the state of closure or lack of closure tabulated in weeks. In the same manner the closure of the foramen ovale was recorded for 500 cases. The plotting of the graph then is evident, as any given point along its contour represents the percentage of the ducti and of the foramina that are closed at any given time.

9. Alexejeff, quoted by Dragendorff (footnote 7).

It was evident that the rapid fall in the first few weeks of life represented the normal closure, but I was more interested in that point where the curve ceased to be normal and tended to become pathologic (charts 1 and 2).

The determination of the exact point of closure appeared to be impossible in the graphs, because there was a deviation from the normal frequency curve so often dealt with in biometrics. Consultation with the statistical department of Columbia University failed to disclose a method for determining this exact point. However, its fine determination is hardly of practical significance, and I submit these graphs for the interest they may have and for their self-interpretation. It was evident

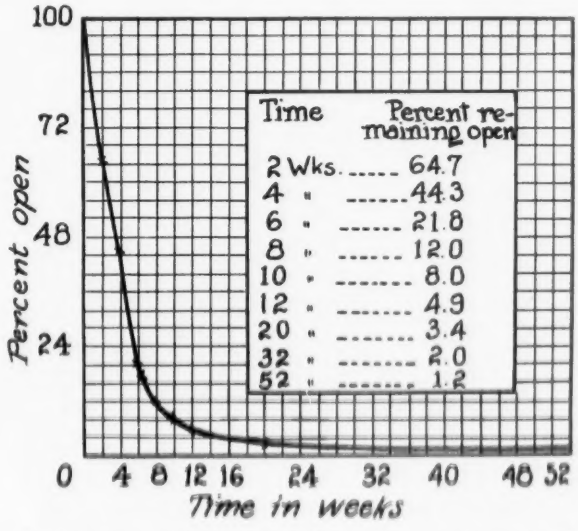

Chart 2.—Normal closing time of the ductus arteriosus in 558 normal hearts of infants from 1 day to 1 year of age.

in the case of the ductus arteriosus that there was a rapid and uniform time of closure up to about 8 weeks of age, at which point there was a marked slowing and deviation of the curve; 88 per cent of the infants showed a closed ductus botalli at the age of 8 weeks.

In the case of the foramen ovale there was a slower descent of the curve until a point at about the twelfth week was reached, where 87 per cent of the cases studied showed a closed foramen. After this point there was a uniform, but slower closing time until at the age of 1 year from 5 to 6 per cent of the infants still had an open foramen ovale. In the great majority of cases the opening admitted only a small probe at the edge of the valve where it had not yet united with the septum atriorum. It is interesting that Hinze[8] believed it possible that final

closure may still occur at the age of 1 year. It is realized, of course, that these fetal passages are physiologically impervious shortly after birth. The futility of attempting to determine this point is readily apparent.

SUMMARY

An attempt was made to standardize the knowledge of the normal anatomic closure of the foramen ovale and of the ductus arteriosus by an anatomic and statistical method.

This closing time of the foramen ovale was found to occur prior to twelve weeks after birth in 87 per cent of 590 normal hearts of infants from 1 day to 1 year of age.

Closure of the ductus arteriosus occurred prior to eight weeks after birth in 88 per cent of 558 normal hearts of infants from 1 day to 1 year of age.

The foregoing figures represent the time of normal unrestricted closure of the foramen ovale and the ductus arteriosus. The patency of the openings after this time is probably compensatory and an expression of other factors in the circulation or constitution that have tended to retard the normal closure.

Case Reports

CHONDRODYSPLASIA

AN UNUSUAL CASE *

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MILWAUKEE

Chondrodysplasia was long thought to be a rare disease in America. Occasional cases were reported under such names as Ollier's disease,[1] chondro-osteoma,[2] multiple cartilaginous exostoses,[3] ossified diatheses, rachitiform enchondrosis and dyschondroplasia. Not until Ehrenfried described the condition in 1915 and collected the available cases in 1917 was its identity well recognized. Since then a number of cases have been reported, and Stocks [4] has worked out a classification of the various forms on the basis of etiology and pathology. The case reported belongs to one of the rarer forms in which multiple enchondromas are present with no exostoses in the patient or the family.

REPORT OF CASE

S. S., aged 2½ years, was admitted to the Wisconsin General Hospital on March 7, 1926, because of bowing of the left forearm and the lower extremities. The birth had been normal, and no one had observed any deformity during early infancy. The child did not creep for over a year; at a considerably later date she walked with a wabbling gait. The deformities were first noticed at this time. No change had been observed in the degree of deformity. The child had always been pale but had had none of the diseases of childhood.

All of the grandparents were normal, and none was of short stature. The parents were living and well and had no deformities. They were intelligent Polish people. In response to detailed questions, they replied that none of their six children who had died in infancy had had deformities or tumors. The patient

* Submitted for publication, Feb. 7, 1930.

* From the Milwaukee Children's Hospital.

1. Thomason, T. H.: Ollier's Disease, Texas State J. Med. **23**:721 (March) 1928. Chrysopathes, J. G.: Beitrag zur sogenannten Ollierschen Wachstumsstörung, Ztschr. f. orthop. Chir. **51**:177, 1929.

2. Percy, N. M.: Multiple Chondro-Osteoma, Surg. Gynec. Obst. **20**:619 (May) 1915.

3. Gibney, V. P.: Multiple Exostoses, M. Rec. **10**:300, 1875. Lewin, Philip: Multiple Cartilaginous Exostoses, Surg. Gynec. Obst. **45**:48 (July) 1927. Ehrenfried, Albert: Multiple Cartilaginous Exostoses, J. A. M. A. **64**:1642 (May 15) 1915; Hereditary Deforming Chondrodysplasia, ibid. **68**:502 (Feb. 17) 1917.

4. Stocks, Percy: Hereditary Disorders of Bone Development, London, Cambridge University Press, 1925.

had five sisters and two brothers. All were examined carefully, roentgenograms being taken when indicated, and none of them showed a trace of osseous maldevelopment.

A physical examination in 1926 yielded no positive observations other than anemia, three carious teeth and the skeletal deformities. The patient walked with a waddling gait and with the right lower extremity slightly in advance of the left. There was a bilateral anterolateral bow-leg which was more marked on the right side, with relative valgus of the feet. At both wrists there was an enlargement of the radial epiphyses, and on the left an enlargement of the radius above the

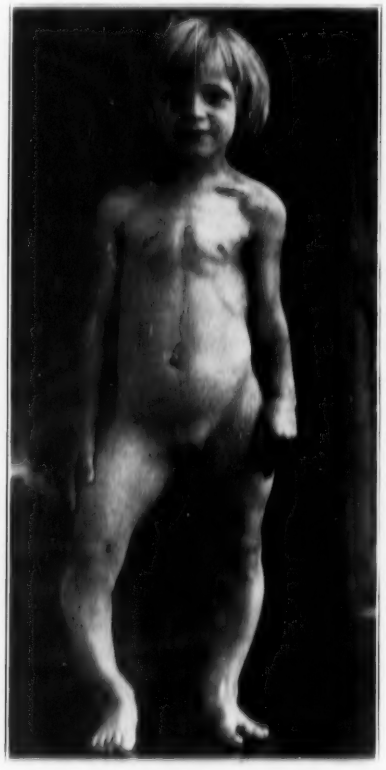

Fig. 1.—Patient at the age of 5. The deformity of the left wrist and both lower extremities is apparent.

epiphysis with a marked abduction deformity at the wrist. The right femur was outwardly rotated 30 degrees and the left 45 degrees. There was broadening of the lower ends of the tibiae.

Roentgen examination established the presence of a mild case of rickets, but disclosed also involvement of many of the bones by another process. The left radius was shorter than the right, and its distal end was bulbous and mottled. Irregular, gouged-out, mottled areas were present in the lower ends of the femora and in the upper end of the left, and at both ends of the tibiae. Some of the phalanges and the pelvis were also involved. From the roentgen evidence of cartilage islands at the epiphyses, a diagnosis of dyschondroplasia was made.

Laboratory examination showed the urine to be normal. The hemoglobin was 72 per cent, with an erythrocyte count of 4,660,000. The leukocyte count was 10,000, with 50 per cent neutrophils, 2 eosinophils, 39 small lymphocytes, 5 large lymphocytes and 4 transitional cells. The Wassermann reaction of the blood was negative. There were 11.6 mg. of calcium and 5.8 mg. of phosphorus in 100 cc. of blood. The coagulation time was 3½ minutes. Subsequent examinations varied only in the appearance of an occasional trace of albumin in the urine, and in an increase in the white blood cells. The latter reached a count of 13,800, with 69.5 per cent neutrophils.

On Aug. 26, 1929, the patient was seen at the Milwaukee Children's Hospital and was again examined. She walked with a limp on the right, with the right lower extremity markedly bowed and in abduction and flexion. She stood with the pelvis abducted to the left and with a right total scoliosis. This was obliterated by bending forward. The left hand was in radial abduction at the wrist, and here the end of the radius was enlarged. The costal margins flared outward, and there was a well marked Harrison's groove. Over the anterior end of the left sixth rib there was a rough enlargement of the bone. There was some thickening of the bones on either side of the knees, but there were no palpable knobs or tumors. Otherwise the results of physical examination were negative.

Motion at the ankles and knees was normal.

Hip Motions	Right	Left
Flexion	140	140
Abduction	60	40
Adduction	50	50
Rotation outward	50	55
Rotation inward	0	60

Measurements	Right, Cm.	Left, Cm.
Anterior superior spine to medial malleolus	45.5	46.5
Circumference of the calf	20.3	21.5
Circumference of the knee	21.5	21.5
Circumference of the thigh	27.0	26.8

Roentgenograms were taken of all the bones. Those showing abnormalities are reproduced. The illustrations show numerous cartilage islands in the pelvis, the ribs and the ends of the long bones.

COMMENT

In 1900, Ollier reported a similar condition, with a unilateral distribution of the lesions.[5] For a time after that, such cases were called by his name. Limitation of the dysplasia to one side of the body, however, seems to be merely an interesting variation.[6] Not all of Ollier's cases were entirely unilateral. Many of the lesions that he described were exactly similar to those found by others when the involvement was bilateral and even symmetrical.[7] Stocks took no account of distribution in his classification.

5. Ollier, L. X. E. L.: Rev. de chir. **21**:39, 1900.
6. Chrysospathes (footnote 1, second reference).
7. Thomason (footnote 1, first reference).

Fig. 2.—Anteroposterior view of the lower extremities. The metaphyses are characteristically elongated, with irregular islands of cartilage distributed throughout them. The bowing is due to rather sharp angulation at the metaphyseal abnormality.

Fig. 3.—Anteroposterior view of the left forearm, showing the characteristic cystlike enlargement of the distal end of the radius. The bone is uniformly peppered with areas of decreased density in this region. Interference with the growth centers has resulted in shortening. Note the involvement of the phalanges.

Widening of the metaphyses is a common observation. It may be observed in the tibiae and femora (fig. 2). The bulbous enlargement of the left radius (fig. 3) is exactly similar to lesions of the long bones described by Thomason,[7] Ehrenfried,[8] Ord,[9] Jansen[10] and Cole.[11] Curvature of the long bones is of almost invariable occurrence. There

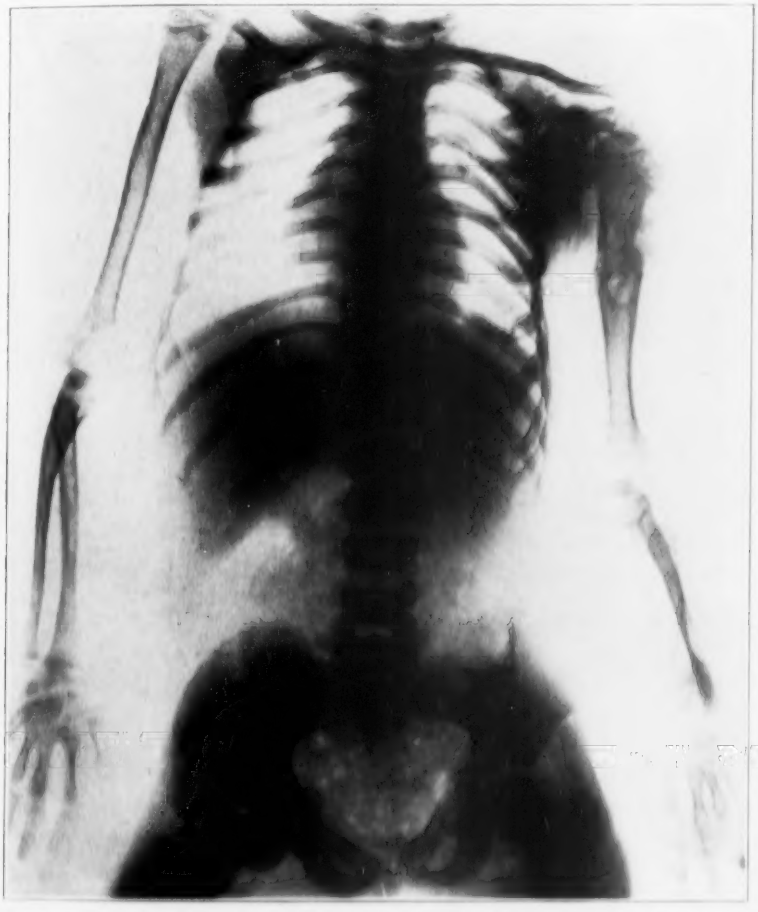

Fig. 4.—The dissemination of the lesions should be noted. The left humerus, scapula and eighth rib are involved as well as the entire pelvis and both femora.

8. Ehrenfried (footnote 3, third reference).

9. Ord, A. G.: A Case of Hereditary Deforming Chondrodysplasia, Lancet **2**:178 (July 25) 1925.

10. Jansen, Murk: Dissociation of Bone Growth, The Sir Robert Jones Birthday Volume, 1928, p. 43.

11. Cole, W. H.: Chondrodysplasia, Surg. Gynec. Obst. **42**:359 (March) 1926.

is frequently impairment of motion at one or more joints. Involvement of the pelvis is not uncommon.

Examples of multiple exostoses have been more or less common and early suggested a descriptive name for the condition. It is less common to find dysplasia at the epiphyses without exostoses, as in this case. The present tendency is to group all of the cartilage dysplasias under the name chondrodysplasia. Stocks supplied a rational classification [4] based on heredity and pathology. It is briefly as follows:

I. Multiple exostoses
  (*a*) History of heredity
  (*b*) No heredity evident

II. Enchondromas
  1. Associated with exostoses in the same person or his family
    (*a*) Heredity evident { single / multiple
    (*b*) No heredity evident { single / multiple
  2. Without associated exostoses { single / multiple

III. Isolated exostoses with no evident hereditary factor

IV. Cranial exostoses
  (*a*) Relatives affected
  (*b*) No hereditary factor

V. Subungual exostoses

VI. Exostoses of the heel

VII. Pseudo-exostoses: riders' bone, etc.

The history and clinical and roentgen observations place this case in group II *2*.

The question of etiology is an interesting one. The similarity to achondroplasia has been observed.[12] There is a marked familial tendency,[13] with a predominance of affected males.[14] Short stature may be a latent manifestation of the disease.[15]

Several theories as to causation have been suggested, but none has been held for long. Murk Jansen [10] considered the phenomenon to be a dissociation of bone growth and especially a retardation of the differentiation of the cartilage cells. This dissociation he attributed to a disturbance of the central elements of the sympathetic system, with resulting vascular spasm and local anemia.

12. Lewin (footnote 3, second reference).

13. Boorstein, S. W., and Hirsch, Henry: Multiple Cartilaginous Exostoses, Am. J. Surg. **6**:194 (Feb.) 1929.

14. Campbell, H. E.: Hereditary Deforming Chondrodysplasia, J. Bone & Joint Surg. **7**:982, 1925.

15. McFarland, Joseph: Hereditary Deforming Chondrodysplasia, Surg. Gynec. Obst. **48**:268 (Feb.) 1929.

Ehrenfried, whose later work[16] furnished an excellent discussion with a review of the literature, ascribed the changes merely to "a disturbance of the bone-forming cartilage."

There has been no treatment suggested. Fractures at the site of the enchondromas heal readily and there is no contraindication to osteotomy, which should be performed for the correction of deformity. Exostoses should be removed when troublesome.

SUMMARY

1. A case of chondrodysplasia without exostoses is reported.

2. There was no familial factor.

3. Many of the cartilage bones were involved in a dysplasia, with islands of cartilage in the osseous tissue near the growth centers.

4. Curvature of the long bones and impairment of joint function resulted.

5. The condition was coincident with a mild case of rickets, but no clue was furnished as to the etiology.

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16. Ehrenfried (footnote 3, fourth reference).

SUBCUTANEOUS RUPTURE OF THE STOMACH *

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AND
IRWIN SCHULZ, M.D.
MILWAUKEE

Subcutaneous rupture of the normal stomach is relatively rare. In a complete review of the literature, Glassman [1] was able to collect only fifty-three cases, and he added to this number two of his own. He classified these into three groups. The first group included cases due to severe or moderate trauma, of which there were thirty-two. The one outstanding symptom was shock. However, over 50 per cent showed hematemesis. The second group included those cases in which rupture occurred following very slight trauma. Glassman felt that distention of the stomach was the important predisposing factor in this type. In the third group were cases of spontaneous rupture. Of the fourteen cases collected, all showed a history of overdistention of the stomach due to either overeating or obstruction at the outlet.

REPORT OF CASES

CASE 1.—A girl, aged 17 months, entered the hospital on Feb. 5, 1929, in a moribund state, having been ill for four days. At the onset, her chief symptoms were obstipation and apparent abdominal pain. Following an enema and administration of castor oil, vomiting and a slight diarrhea developed. Examination demonstrated a markedly distended abdomen with visible peristalsis. There was a secondary anemia and a temperature of 102 F. The child died several hours after admission.

An autopsy, performed six and one-half hours after death, revealed a terminal pneumonia. There was an exudate throughout the peritoneum. Twenty inches below the pylorus there was an obstructing fibrous band with distention above and collapse of the bowel below this point. On the lesser curvature of the stomach there was a very ragged hole with a collection of stomach contents about this region.

There was no history of injury in this case. The rupture of the stomach must have been spontaneous, probably secondary to the upper intestinal obstruction. Microscopic section showed no evidence of ulceration near the site of rupture.

CASE 2.—A boy, aged 3 years, entered the hospital on Aug. 3, 1929. Twenty-four hours before admission fever and difficulty in breathing had developed. Several hours later, there was an onset of projectile vomiting. One hour before

* Submitted for publication, Feb. 14, 1930.

* From the Milwaukee Children's Hospital.

1. Glassman, Oscar: Ann. Surg. **89**:247 (Feb.) 1929.

Fig. 1 (case 1).—Spontaneous rupture of the stomach at the lesser curvature.

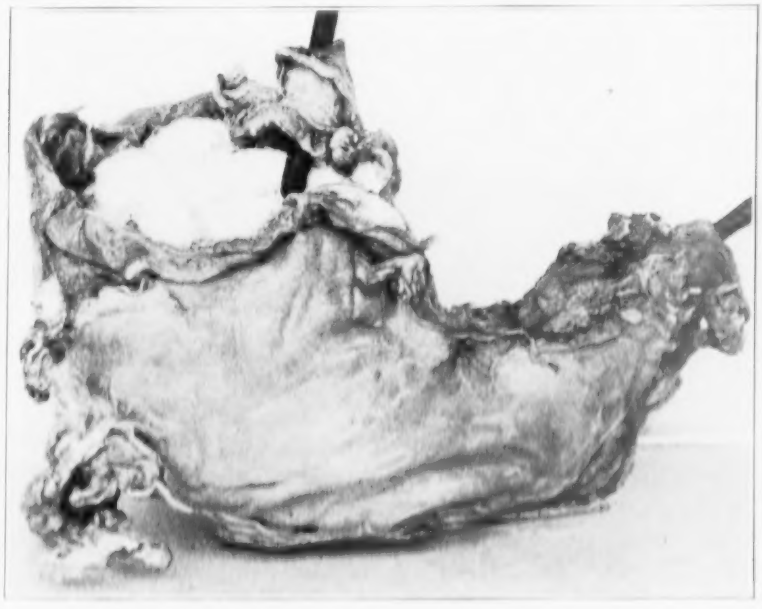

Fig. 2 (case 2).—Rupture in the fundus of the stomach following slight trauma.

entry, he had a convulsion of one minute's duration. Examination revealed an acutely ill child breathing heavily. The tonsils were hypertrophic and an angry red, with a gray, specked exudate. There was slight rigidity of the neck. The temperature was 103 F.; the pulse rate, 112, and respirations, 40. A culture from the throat showed many short-chained streptococci. The child's condition grew progressively worse. Convulsive movements, a positive Kernig sign, and a contralateral Brudzinski sign developed. The spinal fluid was under marked pressure, but it was clear and showed no growth. Three days after admission, respiratory paralysis developed, and artificial respiration was instituted. Oxygen therapy was employed, but the child died shortly after. The diagnosis was septicemia.

Autopsy, performed nine and one-half hours after death, showed that the child had had encephalitis. A blood culture from the heart demonstrated *Streptococcus viridans*. The child had a hydro-ureter on the left side. There was a large opening in the fundus of the stomach adjacent to the esophagus. Microscopic section examination revealed no evidence of ulceration.

In this case, we cannot discount the trauma incident to the artificial respiration, however slight it may have been. The debility due to the septicemia was the most important predisposing factor. There may have been a distention of the abdomen, although there was no objective evidence of this.

SUBCUTANEOUS FAT NECROSIS

REVIEW OF THE LITERATURE*

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AND
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Subcutaneous fat necrosis is also called by the following terms: ischemic fat necrosis, traumatic fat necrosis of the new-born, pseudoscleroderma, sclerema neonatorum, scleroderma neonatorum, curable induration of the skin of the new-born, adiponecrosis subcutanea neonatorum, necrosis adiposis neonatorum, erysipelitis infantum, Verhärtung des Zellgewebes, Subcutane Fettgewebenecrosen beim neugeborenen, fettsklerose im säuglingsalter, Hautsklerom, sclerema dei neonati, sclérème des nouveau-nés, endurcissement du tissu cellulaire, induration cutanée curable des nouveau-nés, cytostéatonecrose du tissu sous-cutané, sclérème adipeux en plaques.

Under this varied nomenclature is described a condition of the skin in the new-born which is manifested by an area of pink or pinkish-blue discoloration, variable in size and circumference. The edges, sharply defined, may be slightly raised or flat, and the consistency is not unlike hard, cold dough, or as has been described, "like the dead half frozen foetus." The skin does not pit on pressure. When grasped en masse, the skin and the subcutaneous tissue adhere, and when gently pinched, the skin puckers, simulating the peau d'orange. Pinching causes no pain. The lesions are neither painful nor tender. The soft parts of the body are usually involved, i.e., the cheeks, the shoulders, the upper parts of the arms, the upper part of the back, the buttocks and the adjacent parts of the lumbar region and the thighs. Two cases were seen presenting this clinical picture.

History.—H. Z., an infant girl, was born at the G— Hospital, on Sept. 19, 1928, a normal, full term child. The birth weight was 7 pounds and 10 ounces (3,458.7 Gm.). She was the eighth child of a poor family, and her seven brothers and sisters were well. The mother, aged 44, had not been pregnant for seven years. She had had normal labor in all her pregnancies, and was in excellent physical health. The Wassermann reaction was negative. The patient was borne through a normal pregnancy, not unlike the previous seven. Labor lasted not quite eight hours, no instrumentation was necessary and there was no asphyxia. On the sixth day, while washing the baby, the nurse noticed a small area of pinkish,

* Submitted for publication, Jan. 30, 1930.

† From the Pediatric Clinic, Beth Israel Hospital.

hard skin on the right buttock. Note of this appeared on the hospital record. A solution of magnesium sulphate was applied and on the tenth day, mother and child were dismissed.

The child was brought to our clinic, on Oct. 22, 1928, when she was 1 month and 3 days old. Her weight was 9 pounds and 2 ounces (4,139.1 Gm.). She had gained 1 pound and 8 ounces (680.4 Gm.) since birth. The temperature was 99.4 F. On examination, the patient was found to be a well developed, breast-fed, normal baby, with no apparent defects. There was an area of indurated pinkish-blue skin which extended over the entire right buttock and reached down to the middle of the right thigh. It spread around the outer surface to the middle of the anterior aspect. The upper border was just above the posterior superior dimple and reached across the sacral region to the left buttock. It was roughly symmetrical on the left side with that on the right except that it did not quite reach to the middle of the left thigh and did not cover as much of the anterior aspect. On the outer side of the calf of the right leg there was a patch 1 inch (2.5 cm.) in diameter, and on both deltoid areas there were small patches. These indurated areas did not pit on pressure and were not tender or painful. The skin was slightly raised, the margins were sharply defined and the masses had a hard putty or dough-like consistency. The mother stated that there had been no spreading for a week, i.e., starting from a small plaque about 1½ inches (3.7 cm.) in diameter the condition had spread rapidly to the present size in about two weeks, then remained stationary.

Physically and dietetically, the child continued to do well. She gained weight rapidly. The chemical and laboratory tests gave normal results. A roentgenogram of the area was found negative. On one occasion the temperature was 97 and once 101.4 F., but usually it was about 99 F. The condition remained the same until November 28, when it began to recede slowly. How long the recession actually took we do not know because the mother did not return to the clinic for some time. She later told us that the entire discoloration and induration had disappeared before Christmas (1928).

The child was seen again at the age of 15 months. She then presented mild rickets with flared ribs, pot belly, pallor and enlargement about the wrist joints. She had eight teeth. She had held her head up at 4 months of age, stood up at 9 months and was just beginning to walk. Except for a slight cold in the spring and a mild diarrhea lasting four days in the summer, she had had no illness.

Case 2.—*History.*—I. N., a boy, was born in a private sanatorium on Jan. 14, 1929. Records of his birth were not complete. The mother was a highly neurotic, irritable person, aged 28 years, poorly nourished, with a chronic cardiovalvular disease, mitral regurgitation. There was one previous pregnancy four years before presentation which was attended by a difficult labor and required the use of forceps. During the gestation period, with the patient, the mother was markedly edematous and suffered from dizzy spells, but at no time did she take any medicine or stay in bed. The urine showed only traces of albumin. The duration of labor was less than six hours. Delivery was spontaneous with no untoward asphyxiation and no undue spanking, though the baby was spanked a little to induce crying.

On February 26, the child was seen by one of us. The complaints were fever, with running nose for three days, cough for one day, and redness and hardening of the skin for about three and one-half weeks. The redness of the skin began when the child was 16 days old. There was an irregular patch on each buttock, the area on the left being almost twice as large as that on the right. These spread rapidly in a few days, became confluent and remained the same size for almost three weeks. Four days before the child was presented for observation, it was

feverish and had a slight discharge from the nose. The temperature rose slowly, and on the day that the child was seen the temperature had been 104 F. A diagnosis of erysipelas was made by the attending physician.

Physical examination revealed a plump child, 6 weeks old, weighing 9 pounds and 10 ounces (4,365.9 Gm.). The fontanel was open, the nose discharging, the lips dry, and the tongue coated. The patient's throat was markedly congested, the tonsils engorged and a posterior nasal drip was present. The heart presented no abnormality. The lungs showed a few diffuse moist râles. Respirations were 60 per minute, there was an occasional cough, and the temperature was 103.6 F. On both buttocks, extending well upward into the lumbar region and downward to the thighs, around the outer aspects of the thighs and ending at the antero-external border, was a bluish-red indurated area, very slightly raised above the surface of the skin, very sharply and markedly defined, neither hot nor tender and which did not pit on pressure. The entire doughlike mass lifted as in one piece and when grasped firmly produced a typical peau d'orange. The left buttock was covered more than the right, and the induration extended lower on the left thigh. Further examination revealed another area on the left cheek about the size of a dime. This was definitely indurated, but it was not raised and the color could not be discerned because the face was flushed.

The usual treatment for nasopharyngitis was instituted, and on the fourth day the temperature returned to normal. The skin condition was treated with prolonged warm baths. The child gained weight and did well. The temperature was always between 98 and 99 F. Toward the end of March, the skin lesions began to clear, and on April 6 the induration had disappeared entirely, having lasted nearly ten weeks.

Medical literature presents many cases of a similar nature. The condition observed in these two cases is so typical and characteristic that the only plausible diagnosis tenable is subcutaneous fat necrosis.

REVIEW OF THE LITERATURE

This condition was described in the early part of the eighteenth century by Usembenzius.[1] In an exhaustive review of the subject published in 1895, Ballantyne[2] was able to refer to 157 individual articles and 70 monographs and texts. He reviewed all that was written on the subject up to that time. From then until today, the status of the knowledge of the subject has not changed much. There is still confusion as to terminology. The etiologic factors are still speculative. The chemical changes in the tissues, especially the composition of the deposited crystals, are still debated. Many cases were reported from Italy and Germany, fewer were reported from England, and in the United States the condition has been comparatively rare.

Etiologically, many views and theories have been propounded. Ballantyne[2] gave a complete résumé of the earlier theories, but in view of the more recent observations these must be discarded. The most

1. Usembenzius, quoted by Abt, I. A.: Pediatrics, ed. 2, Philadelphia, W. B. Saunders Company, 1924, p. 419.

2. Ballantyne, J. W.: Diseases and Deformities of the Foetus, Edinburgh, Oliver and Boyd, 1892-1895, vol. 2, p. 1.

interesting of these theories was that of L. Somma in 1875, later taken up and modified by G. Somma in 1892. They believed that the effect of cold on the body was instrumental in producing the subcutaneous fat changes. Their contention was that there must be some change in the equilibrium between the heat and cold centers, or a neurosis of the thermic centers, and along with this, when there was a lowering of the body temperature, "there followed either oedematous infiltration of the subcutaneous cellulo-adipose tissue, or an induration of the same or both."

Reasoning that the lowering of temperature was a causative factor, Langer [3] suggested that there is a diminution of the olein content of the tissues and that the melting point of the subcutaneous fat was raised. If then the body is chilled, the fat would be crystallized out. Knöpfelmacher [4] showed that the olein and iodine values of the child are diminished and that they attain adult figures at about 12 months of age. In proportion to the rising figures in these values, the melting point of the fat which is high at birth, falls to the adult level as the child approaches its first birthday. Knöpfelmacher believed that this nature of the fat, plus a lowering of the body temperature, was the direct cause of this disease. Thiemisch [5] was able to confirm that there was a diminution only in the olein content. He could not show the return to normal figures of the adult and he thought that the iodine content of the tissues of sclerematous and normal children were alike. Siegert [6] claimed that since Thiemisch found the iodine values alike, the olein values could not be varied and judged the fact that olein is more readily oxidized as a mere hypothesis. Miura [7] and Sarvonat [8] claimed that since there is no difference in the iodine and olein values in the fat of normal children and those with fat necrosis, the olein content and the lowering of body temperature were not causative in the production of subcutaneous fat necrosis. Bayer,[9] working along the same lines as Knöpfelmacher, showed a diminution in oleic acid and thought that a pathologic reduction of this was the direct cause of the malady. Smith [10] examined some indurated tissue and some apparently normal tissue of the same child and found them to be alike. He, therefore, concluded that the reduction of oleic acid was not instrumental in producing subcutaneous fat necrosis. This question as to whether the iodine value

3. Langer, L.: Wien. med. Presse **22**:1375, 1881.
4. Knöpfelmacher, W.: Jahrb. f. Kinderh. **40**:177, 1897.
5. Thiemisch, M.: Ztschr. f. physiol. Chem. **26**:189, 1898.
6. Siegert, F.: Beitr. z. chem. Phys. u. Path. **1**:183, 1902.
7. Miura: Japan. Ztschr. f. Dermat. u. Urol. **5**:412, 1905.
8. Sarvonat: Arch. d. méd. d. enf. **9**:22, 1906.
9. Bayer, R.: Verhandl. d. deutsch. path. Gesellsch. **12**:305, 1908.
10. Smith, C. S.: J. Cutan. Dis. **36**:436, 1918.

and oleic acid content reduction had any effect on the subcutaneous fat was studied by Channon and Harrison.[11] They concluded that a small variation in the olein content of a fat will vary the melting point and yet show no appreciable change in the iodine value. In their studies they also found a reduction in iodine and oleic acid, but the conclusion reached is that the melting point is raised because of the relative "increase in the glycerides of the higher fatty acids, probably palmitin."

The term relative increase of the higher fatty acids is used advisedly. If palmitin or stearin is added to a fat, the melting point is raised. In this condition the palmitin is not increased absolutely. It is increased relatively by a reduction of oleic acid. But what causes this reduction? Gray [12] expressed the belief that there are two probable theories, (*a*) a congenital disturbance in fat metabolism and (*b*) a toxic influence causing damage to the fat cell. Whatever theory may be offered, the fact remains that by increased oxidation or some other metabolic process, the olein is absorbed from the fat cell leaving palmitin, stearin and the glycerides of the higher fatty acids behind. These crystallize out at body temperature because the melting point is higher.

Further along these lines, Lenz [13] contended that cold plays a definite part in the production of subcutaneous fat necrosis. The factors involved are: (*a*) the chemical composition of the subcutaneous fat, (*b*) the intensity of the cold, (*c*) the amount of adiposity, and (*d*) the susceptibility of the organism to inflammatory reaction. The reaction of fatty tissue to cold may remain dormant for some time. According to Lenz, "it is a specific biologic latency in the fetal fat of the new born," and as the fetal fat approaches maturity the reaction to cold diminishes. Fat continues to be formed after the child is born, and until this formation ceases the child is susceptible. Knöpfelmacher recognized this fact and claimed that the condition could not occur after the fourth month of life. He explained it on the basis of rising iodine values. Lenz does not believe that cold per se is the causative factor of the necrosis but rather considers trauma as the true active cause and cold as a variation of trauma.

Trauma at birth has often been considered as a cause. De Vel and Bolin [14] reviewed the literature on this subject and analyzed the cases of Lieberthal, Bernheim-Karrer, Keilmann, Voight and Schultz, Carol and van der Zande, Woringer and Weiner, Marfan and Hallez and Marfan and Debray. In consideration of the large number of difficult

11. Channon, H. J., and Harrison, G. A.: Biochem. J. **20**:84, 1926.

12. Gray, A. M. H.: Sclerema Neonatorum, Arch. Dermat. & Syph. **14**:635 (Dec.) 1926.

13. Lenz, Leo: Ztschr. f. Kinderh. **46**:323, 1928.

14. De Vel, L., and Bolin, Z. A.: Traumatic Necrosis of Subcutaneous Fat of New-Born Infant, Am. J. Dis. Child. **37**:112 (Jan.) 1929.

labors and asphyctic children and the relatively few cases of subcutaneous fat necrosis, it is difficult to conceive that trauma itself is the direct cause. Bernheim-Karrer [15] expressed the opinion that pressure or injury is not alone the causative agent, because whether the injury is slight or severe, the clinical picture obtained is the same. He expressed the belief that the chief injury is due to the cleavage of fat by the action of a lipase either from the injured skin or from the blood serum.

Finklestein and Sommerfeld [16] did not consider the subnormal temperatures and the chilling of the fat as a cause of necrosis. They usually found fever, and they believed that the condition was due to a change in the colloids of the tissues.

The true etiology of the condition cannot definitely be ascertained from this mass of conflicting ideas and opinions, though there is no doubt that we are dealing with an inflammatory process. Histologic sections, described by many observers, show that the trabeculae of the subcutaneous tissue are markedly increased. Fat globules, some partly filled, are seen between these trabeculae. Adjoining these fat globules and even surrounding them, as judged by serial sections, are seen slits or clefts in the trabeculae. It appears that in the paraffin process something has been dissolved out of these spaces, and it is so because in frozen sections these clefts harbor acicular, highly refractive crystals which are arranged like rosettes or sheaves. Occasionally, the staining shows a deposition of lime salts, and throughout the trabeculae is seen round cell infiltration with a few leukocytes. In contact with the crystals are seen giant multinucleated cells. Whatever the cause of the production of these crystals, whether it is the increased oxidation and absorption of the olein or some other cause, they act as foreign bodies in eliciting the giant cells. There is still controversy as to the chemistry of these crystals. Channon and Harrison [11] called them glycerides or crystals of neutral fats. McNee [17] agreed with them and believed them to be "neutral fats, either palmitin or stearin or both" or the glycerides of higher fatty acids. Gray [12] concurred in this opinion. Schultz [18] thought them a palmitin-stearin mixture. Smith [10] considered them as fatty acids, and Lecène and Moulonguet [19] believed them to be soaps. Carol and van der Zande [20] thought that the crystals were cholesterol

15. Bernheim-Karrer, J.: Ztschr. f. Kinderh. **42**:658, 1926.

16. Finklestein and Sommerfeld: Monatschr. f. Kinderh. **25**:105, 1923; abstr. J. A. M. A. **81**:345 (July 23) 1923.

17. Harrison, G. A., and McNee, J. W.: Arch. Dis. Childhood **1**:63 (April) 1926; **1**:123 (June) 1926.

18. Schultz, quoted by De Vel and Bolin (footnote 14).

19. Lecène and Moulonguet, quoted by C. S. Smith (footnote 10).

20. Carol, W. L., and van der Zande, F., quoted by De Vel and Bolin (footnote 14).

esters, and De Vel and Bolin [14] expressed the opinion that they probably are cholesterol esters mixed with fatty acid crystals. They reached this conclusion because they obtained double refraction "with a cross."

The course of the condition is fairly constant. It starts in the first few weeks of life, though it may be delayed until the fourth month when fetal fat reaches maturity. It develops and spreads rapidly and then remains stationary for two to three months. It may go on to cyst formation as described by Fabyan,[21] Harris,[22] Keilmann [23] and Kohnstam and Herbert.[24] The condition is benign and has no effect on the general health and nutrition of the child. It clears up spontaneously leaving no after-effects.

As was histologically shown by Ballantyne [2] and others after him, the condition is a clinical entity. The color, texture and induration of the skin is characteristic. The lack of marked rise in temperature and the physical well being of the child must also be considered. Scleroderma should not be confused with this condition because the skin is yellowish, waxy and parchment-like. The muscles may be involved, whereas in this condition they are never involved. Scleroderma involves the chest and the distal parts of the extremities, while in subcutaneous fat necrosis the buttocks, lower part of the back and the proximal parts of the extremities are affected. Cockayne [25] fully described scleroderma. Considering his case as an example, confusion as to the two conditions should not arise.

Erysipelas is readily differentiated by the systemic reaction. The high temperatures, the toxic aspect of the patient, the heat and the turgidity of the skin will readily differentiate the two, even though at first sight the skin in both conditions looks alike. Erysipelas has not the indurated feel of the skin that is found in subcutaneous fat necrosis.

Benjamin's [26] case of scleroedema neonatorum is typical of that condition, a true subcutaneous edema depending on some organic condition. The shiny tenseness of the skin, the pallor, the distribution of the swelling and the characteristic pitting on pressure leave no doubt that it is an entity distinct from subcutaneous fat necrosis.

SUMMARY

Two cases of subcutaneous fat necrosis are reported with a review of the literature. The early onset, the localization, the symptoms and

21. Fabyan, M.: Bull. Johns Hopkins Hosp. **18**:349, 1927.
22. Harris, F. G., in discussion on Lieberthal's Case, J. Cutan. Dis. **36**:29, 1918.
23. Keilmann, K.: Ztschr. f. Kinderh. **33**:298, 1922.
24. Kohnstam, G. L. S., and Herbert, F. K.: Arch. Dis. Childhood **2**:349, 1927.
25. Cockayne, E. A.: Brit. J. Child. Dis. **13**:225, 1916.
26. Benjamin, E. L.: Arch. Pediat. **41**:209, 1924.

signs and the mode of termination are unlike any other cutaneous or subcutaneous entity. The etiology is involved in a maze of theories. Studies of anatomic and biochemical changes of the subcutaneous fat have yielded conflicting results. We regret that we could not obtain a biopsy in our two cases. Further clinical, histologic and biochemical studies may elucidate many obscure points in this interesting disorder of early life.

Progress in Pediatrics

NEPHROSCLEROSIS (CHRONIC INTERSTITIAL NEPHRITIS) IN CHILDHOOD

WITH SPECIAL REFERENCE TO RENAL RICKETS*

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CINCINNATI

(Concluded from p. 145)

SYMPTOMATOLOGY

The general symptoms of chronic interstitial nephritis in childhood will be discussed and, in addition, the special manifestations of bone changes which accompany a large number of cases.

In the literature, especially that contributed by the older writers, an attempt is made to differentiate between primary and secondary chronic interstitial nephritis. For example, it is brought out by Cockayne[196] that a distinction should be recognized between cases in which there is a congenital defect of abnormally small kidneys with an added inflammation, either intra-uterine or extra-uterine in origin, and cases of chronic interstitial nephritis clinically resembling those of adult life. Just how this differentiation is to be made is not any too clear. It is not possible, except in a few cases, to do this at necropsy, and there is even less during the life of the patient to help the clinician. Practically the important thing seems to be the time of life at which the kidney is damaged. If it is a congenital injury or lack of development, or an injury occurring in early infancy (see section on congenital nephritis and nephritis in newly born infants), the effect on general body development will be greater than if permanent kidney damage occurs later in life.

Age.—The age of onset of symptoms that could be attributed to chronic interstitial nephritis was mentioned in eighty-two of the reported cases. The average age was 7 years and 3 months. In ten more cases, not included in the eighty, the symptoms were said to have dated from birth and in twenty-eight others from early life or infancy. In thirty-two patients in the group with bone changes, the

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average age at onset of symptoms was 5 years and 2 months; in fifty patients in the group without bone changes, 8 years and 5 months.

Sex.—The sex is stated in one hundred and ninety-two cases of interstitial nephritis in children, collected for this paper; ninety-eight were males and ninety-four females; of seventy-four patients of these one hundred and ninety-two with bone changes whose sex is stated, thirty-nine were males and thirty-five females. Of seventy-nine cases of chronic interstitial nephritis in young persons collected by Nettleship,[27] fifty-one occurred in females and twenty-eight in males. This author called attention to the fact that this same proportion in sex difference did not exist in cases of parenchymatous nephritis in which he asserted that males were equally affected, or somewhat more so than females. He also suggested that the reason for the excess of females with interstitial nephritis was linked to the fact that girls were more apt to survive than boys if born syphilitic, and he connected with this statement (which is not proved) another one that "the view that congenital syphilis is often the cause of acute infantile nephritis, usually interstitial, appears to be gaining ground." It has been shown in another place in this publication (see section on syphilis) that the evidence is contrary to the fact that syphilis is responsible for the majority of cases of chronic interstitial nephritis in childhood. Sawyer,[7] in fifty-five cases of chronic interstitial nephritis in young persons, found that twenty-two were in males and thirty-three in females. In forty patients under 13 years of age, 69 per cent were females and 31 were males. In adults, on the other hand, Sawyer affirmed that the proportion of chronic interstitial nephritis was twice as frequent in males as in females. The cases collected in the present publication include many of those reported by Nettleship and Sawyer, and the interpretation seems justifiable that there is no influence of sex in the incidence of chronic interstitial nephritis in childhood or of renal rickets, nor is there any discoverable reason why it should have any influence.

Race.—Probably incidental and explicable on other grounds than racial predisposition is the fact that, as far as can be ascertained, no cases occurred in the colored race. That is, the majority of the reported instances come from England where the colored population is very small.

In one hundred and forty of the case reports on patients over 1 year of age and less than 20 years, the history and physical examination are given in sufficient detail to be acceptable for quotation.

Growth.—In forty-eight cases the history brought out the fact that the patients had always been weakly, delicate or stunted in growth. On physical examination, usually by actual measurements of weight and height, it was demonstrated that seventy-four were decidedly below the

average physical development for their age. Delay in the time of walking occurred in thirteen children. Delay in the eruption of teeth was noted in three instances, marked caries of the teeth in six others. The latter observation is an illustration of the deficiencies of the histories and physical examinations, as the incidence of caries in the average group of well children is certainly greater than the figure given for these children suffering from interstitial nephritis. One would expect, especially in the group with bone changes, to find a high incidence of dental caries.

Mental Development.—From statements in the literature, it is evident that opposing views are held in regard to mental development. On the one hand, it is believed that children with renal infantilism are exceptionally mentally alert, or "bright," "shrewd" and "sharp"; on the other hand, that the mental development is less than the average for age. No actual standards have been employed in the study of this matter. In the collected cases it is specifically stated that twenty-two of the children had normal intelligence or were normally or exceptionally mentally alert; in thirteen children intelligence or mental development seemed less than the average; in the others the subject was not mentioned. Delay in the time of learning to talk occurred in six children.

Sexual Development.—In sixteen children of a total of twenty-five who had reached or passed the age of 15 years, there were evidences of delayed sexual development, such as lack of menstruation, imperfect development of genitalia or breasts, scanty or absent pubic or body hair, or a childish voice.

Polyuria.—Increase in the amount of urine (or enuresis) was noted as a symptom in the history of sixty-four children. In forty-nine children, the polyuria was measurably present while they were under observation. In the terminal uremic state, of course, the urine became scanty. The degree of polyuria in the majority of instances was not excessive, but in a few the amounts of urine passed daily reached 2, 3 or 4 liters, and in one case 6. Often polyuria was an early symptom.

Polydipsia.—Excessive thirst and increased fluid intake was a matter of record or observation in fifty-seven instances. This was often an early symptom and was noticed in infancy about the time of weaning.

Anorexia.—While in the literature attention was frequently called to poor appetite, it was mentioned specifically as a symptom in only about twelve instances. Occasionally, the appetite was excessive, as in a case of Schwarz[209] and as also noted by Guthrie.[12] Abdominal pain and diarrhea occurred in a few patients.

Headache.—In forty-nine instances, the history contained the notation of headache without particular localization as a symptom and it usually occurred later than the symptoms polyuria and polydipsia. Headache was occasionally associated with vertigo and vomiting and resembled migraine.

Vomiting.—Vomiting, the onset of which often occurred about the same time as headache, was a matter of history or observation in forty-seven instances.

Uremia.—Symptoms of uremia developed in sixty-two patients and was a frequent terminal manifestation.

Convulsions.—Most of the patients who died in uremia had terminal convulsions. In several instances, convulsions, presumably uremic, occurred as the first, or as one of the first, manifestations to call attention to the underlying nephritis. Still [28] especially noted this fact. A few convulsions developed with the onset of cerebral hemorrhage and in two or three it may have been a manifestation of tetany. In twelve patients the histories noted dulness, apathy and drowsiness, and these symptoms, in some instances at least, were of a toxic uremic nature.

Tetany.—Carpopedal spasm either alone or accompanying generalized convulsions was brought out in the history of four patients and occurred in five more while they were under observation. (The probable reason for the lack of frequency of tetany in the demonstrated presence of low blood calcium is discussed in the section on pathogenesis of renal rickets.)

Edema.—Slight edema, usually of short duration, was noted in the history or physical examination of twenty-two patients, and more marked or generalized edema in twelve.

Hemorrhagic Tendency.—In twenty patients there was, according to the history or physical examination, some hemorrhagic manifestation such as nosebleed, hemoptysis, melena, bleeding from mucous membranes, purpura or ecchymosis of the skin. This number does not include the patients with hematuria or cerebral hemorrhage. No particular discussion was found in the literature concerning the cause of the hemorrhages. The marked anemia and the high blood pressure usually present are factors to be noted in this connection as are also the sclerotic change frequently found in the blood vessels and the low blood calcium. No evidence is given that the number of platelets is diminished. In a personal case (M. G.) in which marked hemorrhagic manifestations occurred, the clotting time, the bleeding time and the fragility of the red blood cells were normal.

Disturbance of Vision and Retinitis.—Dimness or blurring of vision (diplopia in one instance) was recorded in the history of sixteen patients. In twenty-eight patients, ophthalmoscopic examination showed

evidence of retinitis, in one optic atrophy and in another blurring of the optic disks. No doubt retinitis would have been discovered in many more patients if the eyegrounds had been examined frequently. In the ophthalmoscopic examination of nine patients in the present series of collected cases, the eyegrounds were found to be normal. In Nettleship's [12] eighty-three collected cases of interstitial nephritis in young subjects, there was retinitis in thirty-three; the eyegrounds were examined and found to be normal in ten; in the remainder no ophthalmoscopic examination seems to have been made. Still [28] found that in nine of ten cases of chronic interstitial nephritis in children in which he had examined the eyegrounds there was evidence of albuminuric retinitis or optic neuritis.

Anemia.—In practically every reported instance in which the blood was examined, secondary anemia was found. Pallor and anemic appearance accompanied this and was noted particularly in twenty-nine of the patients.

Pigmentation of the Skin.—A most interesting physical sign is pigmentation of the skin which was remarked on in thirty cases. It was variously described as brownish, yellowish, grayish-yellow or grayish-green discoloration; a dirty sallow complexion; a bronzing or an earthy pallor. Inelasticity, dryness, coarseness of the skin and lack of perspiration were also noted in some cases. The pigmentation may be more marked in the axillary folds and groins or on the flanks and abdomen; it does not involve mucous membranes (Guthrie [13]). The sclera is not involved in the discoloration. The cause of this phenomenon is not clear (see section on pathology [suprarenal]).

Circulatory Symptoms.—In the history of thirteen children are found symptoms such as dyspnea and palpitation which in all probability were part of the circulatory disturbance. Perhaps in this same category may be the four instances in which cough was noted, although this symptom may have been due to a respiratory infection.

Cardiac Enlargement.—Enlargement of the heart on physical examination was found in forty-six patients (see also section on pathology). Cardiac enlargement, while more common in the older patients, was also found in some of the younger ones. In seventeen patients, the aortic second or both second sounds were accentuated. In six, there were cardiac murmurs. Some of the murmurs were due to actual valvular disease, and some, as in Sheldon's case,[111] probably to functional stretching of the valvular rings. In thirteen patients, the notes on physical examination stated that the heart was normal. The cardiac hypertrophy was an efficient one in most instances, at least there was seldom marked failure of compensation, and death was due to uremia and not to cardiac failure.

Arteriosclerosis.—In twenty-four patients, the superficial vessels on palpation were found to be hard, tense, cordlike, rigid, wiry or unduly palpable according to the terminology employed by the author. Symptoms of cerebral hemorrhage occurred in three patients.

Increase in Blood Pressure.—Increase in blood pressure occurred in thirty-three patients; in many of the earlier case reports no such observations were made. The increase in pressure was often great, reaching 190, 250 or 260 mm. of mercury in systole and 130, 190 or 200 in diastole. In some instances, the high arterial tension led to symptoms such as insomnia, night-terrors, nervousness and restlessness.

Examination of the Urine.—In addition to the polyuria previously noted, examination of the urine gave the following results: In seventy-nine instances the specific gravity was low; in one hundred and three, albumin, usually in small amounts, was found; in thirty-three, casts were present; in twenty-three, white blood cells in numbers sufficient to cause notation were recorded; in eighteen, there was hematuria or red blood cells were found in the microscopic examination. It is particularly important to note that albumin may be small in amount and not present on every examination. Casts are probably more frequent than the figure given indicates as in some instances microscopic examination was not performed or if so, on only one specimen of urine.

Kidney Function.—In twenty-six patients, increase in the nonprotein nitrogen constituents of the blood was found. This was often of extreme degree in the terminal stages—blood ureas of 300 to 400 mg. per hundred cubic centimeters being recorded. Schwarz [9a] made the statement that in his experience surgical conditions of the kidney such as infectious hydronephrosis and various congenital malformations have higher nitrogen retention than ordinary medically diseased kidneys. By such function tests as phenolsulphonphthalein excretion, indigocarmine excretion, urea excretion, fixation of specific gravity, etc., renal insufficiency was found in twenty-eight patients. In this connection, attention may be called to the publication of Keith, Wagener and Kernohan [7] on malignant hypertension, as four of their cases are included in the present collected series. In the group they described there was hypertension and frequently retinitis, but relatively good renal function obtained.

The attempt to analyze these symptoms and physical and laboratory signs more accurately than has been done would be futile, even if the number permitted. At least this series of cases is larger than any previously collected and helps to clear up certain hazy ideas which have hitherto prevailed in older publications. The histories and examinations are often incomplete, and many things not recorded are omitted either because of the inherent defects of the free-hand history or because the patients were not completely examined. Of the case

reports on patients with chronic interstitial nephritis, which has just been analyzed, a number were those of patients who had physical signs of renal rickets or bone changes. It is not possible to gain any particularly helpful knowledge of symptomatology or pathogenesis when the latter group is studied separately. Specific mention should be made, however, of genu valgum. This occurred in thirty-one patients. The average age of onset of genu valgum was 9 years in the twenty-four patients in whose histories this fact was mentioned. Three patients developed genu valgum before 2 years of age; four between 2 and 5 years; eight between 5 and 10 years; seven between 10 and 15 years; and four between 15 and 20 years. It may be the first symptom which calls attention to the underlying condition. The youngest age at which it developed was about 6 months (Zanoli[145]), and the oldest 17 years and 6 months. In some cases the deformity came on quickly. Barber[94] especially called attention to this. One of his patients, when about 16 years of age, was sick in bed with an attack of influenza, following which genu valgum developed. Lathrop[114] and Parsons[81] also mentioned the sudden onset. Just why genu valgum should be so frequent is not clear. The act of weight-bearing undoubtedly plays a part, but does not in itself account for the wide difference in the ages at which it develops. Apert[202] stated that in the more severe cases there is a subluxation at the lower epiphysis of the femur. (Bone changes other than genu valgum and their roentgenologic appearance are discussed in some detail in the section on pathogenesis of rickets.)

The symptoms and examination of children with chronic interstitial nephritis may be summarized as follows:

There is no difference in sex incidence; the average age at the onset of symptoms is about seven years, but many patients have symptoms in early infancy; marked retardation of growth is present in almost all patients; mentality may be normal or above the average, but in some patients it is less than the average for age; sexual development is frequently retarded in the patients past the usual age of puberty; polyuria and polydipsia are frequent and early symptoms; anorexia may be a marked symptom; headache and vomiting occur frequently; convulsions, uremic in nature, are sometimes early and often terminal symptoms; tetany is an infrequent symptom; edema, usually slight, is not a very frequent symptom; hemorrhagic manifestations may be present; albuminuric retinitis is frequent; anemia is very constant; pigmentation of the skin is not uncommon; circulatory disturbance is surprisingly infrequent; cardiac enlargement is common; sclerosis of the superficial blood vessels may be present; high blood pressure is very frequently found when examination is made for it; at urine examination there is almost always found low specific gravity and albumin and, less frequently, casts and white and red blood cells; when kidney func-

tion tests are made marked renal insufficiency is usually discovered; genu valgum is a frequent manifestation in those patients who have bone changes.

DIFFERENTIAL DIAGNOSIS

The knowledge that chronic interstitial nephritis occurs in childhood should lead to its recognition. The symptomatology, the physical signs and the diagnostic aids that may be employed have been enumerated in the previous section. It should be easy to distinguish it from other forms of dwarfism and infantilism. The similarity to diabetes insipidus or pituitary disturbance does not extend much beyond the symptoms of polydipsia and polyuria. The severe headache, especially when combined with vomiting, has in some cases led to a faulty diagnosis or suspicion of tumor of the brain. It has already been mentioned in the section on pathology that cystic disease of the kidney and chronic obstruction and infection of the urinary tract may result in

TABLE 5.—*Age at Death*

Age	Nephritis Without Bone Changes		Nephritis With Bone Changes		Total	
	Number	Per Cent	Number	Per Cent	Number	Per Cent
0 to 2 years	12	11.8	0	0.0	12	9.3
2 to 5 years	9	8.9	8	28.6	17	13.2
5 to 10 years	26	25.7	5	17.9	31	24.0
10 to 15 years	39	38.6	8	28.6	47	36.4
15 to 20 years	15	14.8	7	25.0	22	17.0

the same symptoms as chronic interstitial nephritis and for the same reasons, namely, destruction of kidney structure and functional insufficiency. Another condition from which renal rickets must occasionally be differentiated is hyperparathyroidism. Several such cases have been described in which adenoma of the parathyroid glands has been found. Boyd, Milgram and Stearns [204] have reviewed the reported cases and described one of their own in which it was necessary to make the differential diagnosis. They pointed out that the chief distinguishing characteristic is that in renal rickets the blood calcium is lowered and the phosphorus increased, whereas in hyperparathyroidism the reverse is true.

PROGNOSIS

The prognosis of chronic interstitial nephritis in childhood is naturally serious. Fifty of the patients were alive at the time of the report. Of one hundred and twenty-nine patients in whom the age at death was given, the average was 9 years and 9½ months. Certain details are best shown in table 5.

The prognosis of congenital nephritis, or nephritis occurring in very early life, has been referred to in the appropriate section. The entire

group of patients whose case reports were collected in making this study were under 20 years of age at the time they were studied. A few of them were known to have lived to reach the third decade of life. As a rule, the earlier symptoms developed the more serious was the prognosis and the earlier the age at death, but a study of the case reports will show that there were many exceptions to this. The statement of Sawyer [11] that the average duration of life after symptoms were first noticed was about a year is not sustained by the present survey. Almost all of the twenty-two children who lived beyond the age of 15 years had had symptoms before that time. Some authors have attempted to relate prognosis to the onset of genu valgum because of the belief that death occurred in a year or so after its development. Study of the case reports does not warrant this conclusion, as quite a few patients had this deformity for several years. No doubt, however, it indicates a serious kidney insufficiency. The development of retinitis, very high blood pressure, marked nitrogen retention in the blood are all bad prognostic signs.

TREATMENT

There is little to say concerning the treatment for chronic interstitial nephritis in children. One should remember that infection of the urinary tract and calculi in it may be potential sources of destruction of the kidney. It might be possible, too, in an occasional case, to relieve obstruction before much damage to the kidney has occurred. The treatment of symptoms differs in no way from that in adults and, therefore, need not be discussed here. The danger of giving an anesthetic to these children and operating on genu valgum is obvious, and death has occurred under these conditions, as reported by Barber,[44] Naish,[194] Cameron [187] and Paterson.[125] On the other hand, Roth,[140] Evans,[121] Watson-Wemyss [201] and Zanoli [145] described patients on whom double supracondylar osteotomy was performed with no untoward results.

SUMMARY

In studying the literature on nephrosclerosis, it is found that terminology is confusing. The term chronic interstitial nephritis, which has been employed for a long time to describe the essential underlying pathologic process, is more descriptive of an end-result than of a definite entity. It is suggested that for the use of the clinician a simple terminology be adopted somewhat as follows:

Acute hemorrhagic (glomerular) nephritis

Acute edematous (tubular) nephritis (sometimes called nephrosis)

Chronic nephritis which is usually diffuse, but in which glomeruli, tubules, blood vessels or interstitial tissue may be involved to a greater extent than in the remainder of the kidney structure.

Suppurative nephritis which may be acute or chronic
Lipoid nephrosis

It would seem that all cases of actual kidney disease could be grouped etiologically, pathologically and symptomatically under such a classification. The term nephrosis, and especially lipoid nephrosis, should be reserved for a relatively small number of cases in which there have been determined such well defined criteria as changes in the albumin globulin ratio of the blood, increase in blood cholesterol and the demonstration of doubly refractile lipoid bodies in the urine.

That nephrosclerosis (chronic interstitial nephritis) occurs in childhood has been well recognized since 1870. Following that time, many clinicians noted that it was accompanied in early life by stunting of growth and infantilism. Lucas, in 1883, first described the occurrence of late rickets with albuminuria. While reports can be found in which there was evidence that bone changes occurred in patients with nephrosclerosis it was Fletcher, in 1911, who clearly defined the etiologic connection between the chronic kidney disease and the bone deformities. There have been found and analyzed in the present publication seventy-six cases of so-called renal rickets to which have been added two personally observed cases.

It is evident from a study of the literature that there is definite evidence that family predisposition to chronic kidney disease exists.

Intra-uterine nephritis, or nephritis in very early life, may occur. It is possible that in some instances the end-results of this may become manifest in later childhood. That is to say, the damage is not sufficient to cause death at once, and enough functioning tissue remains to carry on until such time as greater demands are made on the kidney by such factors as increased body growth, or the increased functional demand for excretion of waste products, the end-result of tissue destruction by bacterial toxins which occurs during infections, or the elimination of endogenous and exogenous toxins and poisons other than bacterial which add their load to kidney function.

It has taken the advent of the Wassermann reaction to prove that syphilis is an etiologic factor in few if any cases of nephrosclerosis and renal rickets. From a pathologic point of view, congenital syphilis can attack the kidney and cause damage, but it must be seldom that this injury carries over into nephrosclerosis.

Perhaps all the evidence on the subject of infection as related to nephrosclerosis may best be summarized in the statement that acute bacterial infections, especially of a streptococcic nature, may in some cases injure the kidney and cause chronic as well as acute nephritis. Influencing this may be a hereditary predisposition to kidney disease. There remain cases in which chronic kidney disease may be due to causes other than bacterial.

In some instances it seems evident that an acute infection merely precipitated or aggravated symptoms or added to the load which previously diseased kidneys had hitherto carried without much difficulty.

Lead, alcohol, gout and other exogenous and endogenous poisons and toxins are seldom etiologic factors in nephrosclerosis in childhood.

The dwarfism and infantilism that accompany nephrosclerosis in children are not fully understood, but are explained as the effects of the nephritis on the metabolic processes of a young growing organism.

The changes of the bone that occur in cases of nephrosclerosis in early life resemble clinically those of the usual infantile rickets. Enlargement of the epiphyses of the wrist and the costochondral junctions, pigeon-shaped chest, bossing of the frontal and parietal bones and deformities of the extremities may occur. With peculiar frequency, genu valgum is present. By roentgenologic and histologic study, these changes appear somewhat different from those found in infantile rickets, and the shafts of the long bones and the flat bones have greater translucency and a more spongy appearance than is usually seen in ordinary rickets.

In the present article is summarized a number of studies that make plausible the view that in a type of nephritis characterized by a relative or absolute inability of the kidneys to excrete the waste endogenous phosphates from the body, such waste phosphates may be excreted through the intestinal mucosa instead of from the kidneys. It has been repeatedly demonstrated that an increased concentration of phosphates in the food—that is, in the intestinal contents—may interfere with the absorption of calcium, presumably through the formation of insoluble calcium phosphates. An hypothesis is offered that in renal rickets such a shift of the excretion of endogenous phosphorus to the intestines occurs, and that the concentration of phosphorus in the intestine thus increased so blocks the absorption of calcium from the food that the child suffers a true calcium starvation.

From a study of the clinical history and the pathologic picture, it is evident that urinary calculi may cause kidney destruction which leads to a functional insufficiency and symptoms similar to those produced by nephrosclerosis.

Obstruction of the urinary tract interferes with excretion of urine and the metabolites contained in it. It has been present in some of the patients in whom symptoms similar to those of nephrosclerosis developed.

It may be stated that dilatation of the urinary passages is found in chronic infections of them and that destructive changes and overgrowth of interstitial tissue occur in the kidneys in such cases. Such infection develops in the absence of demonstrable obstruction of the urinary tract as well as when this is present. The relation of cause and

effect is not clear, but it may be that in some instances the infection is the primary factor.

Congenital cystic kidney is a condition that may give rise to symptoms similar to nephrosclerosis. It is perhaps of some importance to state that of ten instances in which cystic changes or greatly dilated tubules were found in the kidneys at necropsy, there were nine in which clinical or roentgenologic evidence of bone changes had occurred. That this may be linked up to some particular disturbance of function which the tubules control is at least worthy of speculation.

The symptoms and examination of children with nephrosclerosis may be summarized as follows:

There is no difference in sex incidence; the average age at the onset of symptoms is about seven years, but many patients have symptoms in early infancy; marked retardation of growth is present in almost all patients; mentality may be normal or above the average, but in some patients it is less than the average for age; sexual development is frequently retarded in the patients past the usual age of puberty; polyuria and polydipsia are frequent and early symptoms; anorexia may be a marked symptom; headache and vomiting occur frequently; convulsions, uremic in nature, are sometimes early and often terminal symptoms; tetany is an infrequent symptom; edema, usually slight, is not a frequent symptom; hemorrhagic manifestations may be present; albuminuric retinitis is frequent; anemia is very constant; pigmentation of the skin is not uncommon; circulatory disturbance is surprisingly infrequent; cardiac enlargement is common; sclerosis of the superficial blood vessels may be present; high blood pressure is frequently found when examination is made for it; on examination of the urine low specific gravity and albumin are always found and, less frequently, casts and white and red blood cells; when kidney function tests are made there is usually discovered marked renal insufficiency; genu valgum is a frequent manifestation in those patients who have bone changes.

The prognosis of nephrosclerosis in childhood is naturally serious. In a series of approximately two hundred patients under 20 years of age, fifty were alive at the time their cases were reported; of one hundred twenty-nine in whom the age at death was given the average age was 9 years and 9½ months.

REPORT OF CASES FROM THE LITERATURE

In the following section are abstracts of reports of those cases of chronic interstitial nephritis in which changes of the bone have been described.

Lucas [5] reported on late rickets associated with albuminuria, or the "rickets of adolescence."

The first case described by him was that of a boy 17 years of age who had a pigeon chest, beading of the ribs and an enlargement of the wrists. He had marked pallor and albuminuria.

The second case was that of a boy 15 years of age who had been ailing and growing weaker for twelve months. It was noticed that his knees were bent in. On examination, it was found that he had slight genu valgum, curvature of the spine and slight enlargement of "the growing extremities of the ribs"; the urine contained a large amount of albumin. He was treated with iron phosphate and cod liver oil, and in two months the albumin disappeared.

The third case was that of a boy 12 years of age who had bending of his spine and slight general enlargement of the epiphyses. He was pale and "vacant in manner." After treatment similar to that of the second patient, he seemed to improve.

The fourth case was that of a boy 16 years of age, who had genu valgum on the right side which had been "giving away" for twelve months. He had general enlargement of his epiphyses and a pigeon-shaped chest. His urine contained albumin. He was treated in the same manner as the second and third patients.

The fifth case was that of a boy 15 years of age who had had weakness of his right ankle for some months. He had "spurious valgus" of the right foot and enlargement of the epiphyses of both ankles; his thorax was pigeon-shaped. The urine contained albumin.

Lucas said: "I would suggest the name of rickets of adolescence. It is possible that exception might be taken to the term rickets but I have not the slightest doubt that the condition under consideration is essentially the same as that of early life. Late rickets and albuminuria are too frequently connected to be matters of chance. The discovery of albuminuria renders it easy to give such advice as may prevent these cases from persisting in habits which would cause their deformities to become permanent."

Apparently Lucas did not diagnose these cases as chronic nephritis, and seemed to think that they had a relatively good prognosis. There were no necropsies, and the final results are not stated in any of the cases.

Davis-Colley [8] reported in considerable detail the case of a girl, aged 13 years. The case evidently belongs in the category of those being discussed as at the post-mortem examination rachitic changes in the bones as well as osteomalacia were discovered. The knock-knees and bone deformities, according to the history, began at 9 years of age; fractures had occurred; at necropsy, both kidneys were large; the right kidney pelvis contained a number of angular stones; both ureters were dilated; there was multiple suppuration of the right kidney.

Goodhart [8a] reported several cases of chronic nephritis in children. One of these was that of a girl 10 years of age who had never been strong and whose legs had been crooked ever since she began to walk. For two years she had had polydipsia and polyuria. She was small and had deformed tibiae. From the description of Goodhart, it would appear that she died in an attack of uremia. At necropsy, small kidneys with interstitial changes were found. This case was one of which the notes were furnished by Dr. Henry Ashby of Manchester, and it would not seem that Goodhart had been in any personal way concerned. It is likely that this is one of the cases reported by Ashby.

It cannot be found that in any other way in his chapter than in this quoted case report has Goodhart mentioned changes of the bone in chronic nephritis in

childhood, nor does he discuss any etiologic relation between bone changes and the nephritis.

Hellendall[9] reported two cases of hereditary contracted kidney in sisters in early childhood. One of the sisters had bone changes. The mother had died from chonic nephritis and had had symptoms of nephritis during her pregnancies. The first girl died at 6 months of age. She had always been sickly and was quite athreptic; she had had no particular thirst. She had had a mild attack of measles. At necropsy, the kidneys were found to be small and granular with chronic interstitial changes, and they contained several cortical chondromas; the heart was not hypertrophied.

The other sister, aged 2 years, was weakly at birth; she had had furunculosis of the skin. She had never learned to walk or talk, and was quite feeble. She showed considerable thirst, especially at night; she frequently vomited and her feet had been swollen. She had had a mild case of measles but not scarlet fever or diphtheria. She had marked evidences of rickets; the color of her skin and mucous membranes was pale. The heart was normal. Bronchopneumonia developed. At necropsy, it was found that there was marked atrophic granular nephritis; the heart was not hypertrophied.

Hellendall did not believe that the measles was causative, and argued that the evident chronicity of the process in the infant's kidney suggested an hereditary type.

Sequeira[10] reported, under the title of "A Case of Polyuria," the case of a boy who was first seen when 2 years and 10 months of age. He had been breast fed for fourteen months. At 18 months of age he had had pertussis, and since then suffered from polyuria and polydipsia. He was poorly nourished and weighed only 16¾ pounds (7,600 Gm.). Evident signs of rickets were demonstrated in the shape of the head and in the enlarged epiphyses of the long bones. The urine was alkaline, pale and contained a small amount of albumin. Several months later the child died, and at necropsy the kidneys were found to be large and granular; cirrhotic changes were found on microscopic examination. There was hypertrophy of the left ventricle; the other organs were normal.

Sawyer[11] was able to collect twenty-four instances of chronic interstitial nephritis in young persons; thirteen of these occurred in patients under 10 years of age, eight in those between 10 and 15 and three in those between 15 and 20. One of these patients, a boy, aged 2 years and 5 months, had bone changes; he had habitually passed large quantities of urine, the polyuria being more marked during the five or six weeks before admission to the hospital, during which time also the abdomen became enlarged. He was very thirsty and vomited occasionally. The family history was without significance in relation to the patient's condition. The child had never been breast fed; he had had "fits" when 7 weeks old; there was no history of any contagious disease. On admission, he was found to be rachitic; he had an accentuated aortic second sound; the urine had a specific gravity of 1,002 and contained a trace of albumin, and the average amount passed daily was 33 ounces (976 cc.). He died a few weeks after admission from uremia. At necropsy, the heart was apparently normal; the kidneys were small, and there was atrophy and fibroid overgrowth.

Nettleship,[97] in a paper on "Renal Retinitis in Young Subjects and on the Relative Frequency of Juvenile Interstitial Nephritis in the Two Sexes," reported one case with bone changes. The patient was a boy whose age was not stated; he had rickets and stopped growing at 16 months of age; the head became enlarged and polyuria developed; at 4 years of age the intelligence began to fail; he had scarlet fever at 7 years of age; the tibiae were bent; the urine had a specific

gravity of 1.010 and contained much albumin; there was edema of the feet and hands; neuroretinitis was present; at necropsy, the heart was found dilated, the aortic valves diseased, the right kidney small, cystic with visible healthy structure (macroscopic examination only), the left kidney absent.

Fletcher [18] reported a case of renal rickets in a boy 6 years of age who was said not to have grown since the end of his first year and to always have had polydipsia (at 4 months of age as much as 4 pints [2.3 liters] a day) and polyuria. He had been breast fed for a year and had had no illnesses. The mother had phthisis. Genu valgum developed when the child was 5 years of age. He weighed only 21 pounds (9,500 Gm.) and his height was 31 inches (78.7 cm.); his intelligence was good; he had carious teeth; his heart was normal; his kidneys were palpable; his systolic blood pressure was 75; he had double genu valgum; the testicles were undescended. He passed from 40 to 70 ounces (1,182.9 to 2,070.2 cc.) of urine a day and drank daily about 3½ pints (2 liters) of water; the urine had a specific gravity of 1.005, and a small amount of albumin and occasionally granular casts were present; the Wassermann reaction of the blood was negative. The case was regarded as one of infantilism, associated with or due to chronic renal disease, dating from intra-uterine existence.

Sutherland,[129] under the title of "Infantilism," reported the case of a girl 16 years of age who had been normal in every way until the age of 6 years, when growth ceased and rickets appeared. She had had measles at the age of 2 years. She had the appearance, speech and intelligence of a child 6 years of age; there was distorsion of the bones of the extremities, epiphyseal thickening and a rachitic chest; the urine had a specific gravity of from 1.000 to 1.005, but contained no albumin or casts. Occasionally there was marked retention of urine without discomfort. There was polyuria and polydipsia. The radial and brachial arteries were thickened; the arterial pressure was 120. There were no retinal changes; the skin was pigmented; the heart was somewhat dilated; the Wassermann reaction was negative. Sutherland suggested that contracted kidney was present. This patient was traced by Miller and Parson [205] about ten months after Sutherland's report, when she was found still to have polyuria and polydipsia. She was backward mentally and physically and had not menstruated; her heart appeared normal, but the radial arteries were thickened; the systolic blood pressure was 108; the Wassermann reaction was again negative. The urine was said to be much increased in amount; the specific gravity was 1.001, but there was no albumin, casts or sugar. This case was not considered to be one of chronic nephritis by Miller and Parsons, but diabetes insipidus with infantilism. The authors classified it as "renal infantilism without organic renal disease," and cited from the literature other cases of infantilism in diabetes insipidus. It is included here, however, as a probable case of renal rickets.

Naish [184] reported two cases of renal rickets. The first occurred in a boy 9½ years of age who had been very small at birth. He was breast fed for a year and walked at 10 months of age. He had excessive thirst after weaning. Polydipsia continued and polyuria developed; at 8½ years of age his legs began to bend; at 9 years he weighed only 32 pounds (14,500 Gm.) and was only 40 inches (101.6 cm.) in height. He had been operated on five times for hypospadias. The family history was unimportant. At 9½ years of age he had the appearance of a 4 year old child; his skin was dry and wrinkled and a faded yellow; he had a moderate genu valgum; there was beading of the ribs and enlarged epiphyses at the wrists; he was "bright and attractive but his mental calibre was that of a child 4 years old." One specimen of urine did not show albumin, but he died in a semicomatose condition when about 10 years old; at that time there was partial sup-

pression of urine, and albumin and casts were present. At necropsy, the kidneys were found to be very small and granular, and on section there was the picture of interstitial nephritis; the arteries of the kidneys were thickened; the heart showed moderate hypertrophy of the left ventricle.

The second case occurred in a boy 16½ years of age who had been born at full term, but was very small; he was breast fed for two months; he walked first at 2 years of age; he always remained small; he always had polydipsia and polyuria; he appeared bright but was backward in school; he sometimes had "sick headaches"; his legs began to bend at about 14 years of age. His mother was ailing throughout pregnancy and vomited frequently. The family history was without particular significance unless it was that a brother had congenital heart disease. On examination, he was found to be small (height, 51 inches [129.5 cm.]); his face was "wizened"; his skin was yellowish and inelastic; his voice was high-pitched and small; his testicles were undescended; there was no pubic hair and the genitalia were not developed; he had marked genu valgum; the ends of the bones were not enlarged and rickets was not considered to be active. On admission, the urine did not contain albumin, and its specific gravity was 1.005. He was operated on for genu valgum. After this albumin was found in his urine. About three weeks later, he died after a period of air hunger, drowsiness and suppression of urine. Examination of the kidneys showed changes similar to those in the first case, except that the arteries were not thickened. The heart showed moderate hypertrophy of the left ventricle.

A brief account of a case of Dr. Barnes is mentioned, that of a girl 17 years of age who was markedly infantile in appearance. She was operated on for genu valgum and died shortly afterward with uremic symptoms. Her kidneys were found to be small and fibrotic.

Hutinel[190] described a case which probably was renal rickets in a girl 13 years of age. At the age of 3 years she suffered for fourteen days from headache and vomiting; at 8½ years she was treated for genu valgum; polyuria and polydipsia developed; at 11 years she had albuminuria and edema. When seen at 13 years of age she had rachitic bone changes; the urine was abundant and contained albumin, and the impaired renal function was proved by injection of methylene blue (methylthionine chloride U. S. P.), urea and salt. The author stated that the bone deformities occurred prior to the kidney disorder (although he does not seem to have proved this) and he did not believe that the kidneys were at fault. The bone changes, he stated, resembled osteomalacia as well as rickets. He believed that this dystrophy was caused by alteration of the glands of internal secretion and particularly the hypophysis.

Miller[194] reported a case of renal rickets in a boy about 10 years of age who had had polyuria and polydipsia since birth and whose growth had been slow. The family history was without significance. The patient had had an attack of diarrhea at 5 months of age and measles at 4 years. Knock-knee developed when he began to walk. On examination, the height was found to be only 37½ inches (95 cc.) and the weight 34 pounds (15,400 Gm.). The boy was intelligent, but childish, "in keeping with his size rather than with his age"; he was anemic and had a sallow, wrinkled skin. The knock-knees were demonstrated by pictures. The kidneys were not palpable; there was a marked phimosis and the testicles were small. He passed from 40 to 60 ounces (1,182.9 to 1,774.5 cc.) of urine daily which contained a trace of albumin and granular casts, was sterile and had a specific gravity of from 1.001 to 1.004. The heart was enlarged as demonstrated by clinical and roentgenologic examination; the radial arteries were not thickened but the brachials were quite palpable; the systolic blood pressure was 130; the

Wassermann reaction was negative. The child was under observation for two and one-half years during which time he grew only an inch in stature. He died of pneumonia. No necropsy was performed. (This case as reported in the communication of Miller and Parsons of 1912 [205] gives information additional to that contained in Miller's article of 1912 which has been included here.)

Zundell [206] reported two cases of infantilism, in one of which there were slight changes of the bone. This case was in a boy 13 years of age, who at the age of 3 years had an attack of sore throat which may have been diphtheritic in nature. Polyuria and polydipsia dated from that time. He had had no other illnesses. The patient's father had diabetes insipidus, and a brother had died of this disease. The examination showed a wasted child, whose height was 42 inches (106.6 cc.) and whose weight was 2 stone 1½ pounds (29½ pounds [13,450 Gm.]); the skin was dry; the intelligence fair; the epiphyses were "clearly defined;" the testicles were "childish"; the pituitary fossa appeared normal on the roentgenogram; the blood pressure was 100; the urine had a specific gravity of 1.000 but contained no albumin or casts. This case was considered one of diabetes insipidus and may well have been so rather than one of chronic interstitial nephritis.

Barber [44] reported among others a case in which renal rickets was present. This occurred in a boy 16 years of age who was undersized but not obviously infantile and who was operated on for genu valgum which had developed fairly recently. The urine examined before operation showed a specific gravity of 1.014, but albumin was not detected. Ten days after operation, the boy became comatose and died. At necropsy, interstitial nephritis was found; there was no dilatation of ureters or pelvis of the kidneys; the heart, aorta and other organs were normal.

Porter [138] reported two cases of renal rickets. The first case occurred in a boy whom he first saw at the age of 7½ years because of the chief complaint of rapidly increasing flatfoot and difficulty in walking. The child had always had poor digestion. At one time it was said that albuminuria had been present. On examination, it was found that the patient was exceptionally alert mentally; he was undersized, but well proportioned; there were rachitic thickenings of the wrists, flatfoot, bowing of the femurs, Harrison's groove; physical signs of congenital heart disease were found; the external genitalia were normal; the urine contained albumin; the roentgenograms showed incompleteness of calcification in all diaphyses and absence of ossification in the wrist bones. On subsequent examinations, granular casts were found in the urine and as much as from 40 to 46 ounces (1,182.9 to 1,360.9 cc.) was daily voided; at times as much as 16 to 18 ounces (473.11 to 532 cc.) was voided at one time. The Wassermann reaction was negative. The bone deformities increased in severity. The patient was last seen when over 9½ years of age, at which time there was such bending of the bones of the lower extremities that he could not stand erect.

The second case reported by Porter was that of a boy 6½ years of age. This patient had malnutrition as an infant; he did not walk until 4 years of age and he did not talk until he was 3 years; he had always had nocturnal enuresis; for three years he had had headaches; he had polyuria and polydipsia. For four days before his death he had suffered from chills, abdominal pain and vomiting and was evidently in uremic coma. He was undersized, had a marked rachitic rosary and a Harrison's groove. Both kidneys were palpable; there was malformation of the urethra, "one urethra passing back to the bladder and another ending in a blind sac about half way back." The urine contained albumin and was loaded with pus cells. There were no roentgenologic studies, no cystoscopic examination

was made and necropsy was not performed. The diagnoses were pyelonephritis, congenital malformation of the urethra and renal infantilism.

Barber[124] reported a case of interstitial nephritis with infantilism and rickets in a boy 16 years of age. The family history was unimportant. The patient was probably a 7 months, premature baby and was small and weak; he was not breast fed; he had not had scarlet fever or any other illness; in childhood he became active and intelligent; at 15 years of age genu valgum developed. On examination, he was found to be 47 inches (119.3 cc.) in height and to weigh 46 pounds (20,800 Gm.); his face was not pale; his voice was childish; he had no hair anywhere on his body; his testicles were small; he had marked genu valgum; he had enlargement of wrists and costochondral junctions and in the roentgenograms irregular ossification similar to that of rickets was found; the heart was normal; the brachial arteries were palpable; the systolic blood pressure was 100 and the diastolic 70; the eyegrounds were normal; the urine had a specific gravity of from 1.004 to 1.010, it contained albumin, and the average daily quantity was 51 ounces (1,508.7 cc.); there was thirst, but it was not extreme; the thyroid was normal, and there were no signs of syphilis.

Cameron[187] reported two cases of renal rickets. One case occurred in a girl 15 years of age who was dwarfed and infantile and who had extreme deformities of the wrists and knees, which had appeared eighteen months before. Osteotomy was performed, following which there was suppression of urine, drowsiness and, four days after operation, death. Postmortem examination of the bones and the roentgenograms showed great irregularity of the epiphyseal lines with extensive uncalcified areas in the surrounding bones. The kidneys were represented by a single horseshoe structure; there were numerous cysts and the microscopic changes were those of chronic interstitial nephritis; some atheromatous changes were found on the mitral valve.

Cameron's second case occurred in a girl 17 years of age who had not grown since the age of 9 years. She had marked bone deformities, polyuria and retention of urea. The roentgenograms were similar to those of the previous case.

Fletcher[197] reported a case of chronic interstitial nephritis with some bone changes in a girl 14 years of age who had been weak and backward in development since infancy and had suffered for some time from a severe frontal headache. Micturation had been frequent for many months; she had become much weaker and paler in the last few months; for three days she had been vomiting. She had had measles in infancy and scarlet fever when 12 years of age. The father and mother and seven brothers and sisters were in good health. On admission to the hospital, the patient was found to be small (35½ pounds [16,100 Gm.]), pallid and poorly nourished; her intelligence was good; there were no signs of advancing puberty; the radial arteries were small and wiry; the systolic blood pressure was 240 and the diastolic 190; the left ventricle was moderately hypertrophied and the aortic second sound accentuated; except for a slight degree of genu valgum there was no obvious curvature or deformity of the bones; the urine contained a small amount of albumin (0.3 per cent), some red and white blood cells, a few granular casts, some long chain streptococci, and its specific gravity was 1.010; there was edema of the disks, retinal hemorrhages, pigment proliferation and other evidences of changes which had been present for some months; the Wassermann reaction of the blood was negative; the administration of 5 Gm. of urea did not produce any increase in the urea concentration of the urine. The subsequent course of this case is not given in this report. Later, in a publication of Evans[121] on arteriosclerosis in children, it was stated that the patient died in an uremic convulsion, and at necropsy there was found chronic

nephritis with great interstitial fibrosis and obliterative endarteritis, hypertrophy of the left ventricle and arteriosclerosis affecting the aorta, coronary arteries and carotid vessels. The ureters were somewhat dilated and the bladder somewhat hypertrophied.

Paterson[198] reported three cases of renal dwarfism with rickets. The first occurred in a boy 11 years of age. He had been healthy at birth and breast fed for nine months. He had always been a great drinker of water. At 6 years of age he had an acute febrile illness accompanied by vomiting; at 7 years it was noticed that his legs had become bent and that he was knock-kneed; at 7½ years it was discovered that he had kidney disease. His family history was negative for kidney or bone disease. At 11 years of age he was admitted to the hospital where a fracture and great thinning of the bone substance was found in the roentgenologic examination. He was operated on for the deformity and died in uremia shortly thereafter. At necropsy, the kidneys were found to be extremely small and showed some cystic and fibrotic changes. The only other organ that was abnormal was the heart, which was dilated.

The second case occurred in a boy 1 year and 9 months of age. The family history was without significance. The patient had been breast fed until 11 months of age. He had always been small; he could stand at 1 year of age; at 10 months of age he began to have deformities of the ankles and wrists. When examined, he was found to be undernourished (weight 10 pounds 8 ounces [4,700 Gm.]); he did not talk but seemed intelligent; he had a narrow chest, beading of the ribs, open fontanel and a Harrison's groove; the femur, tibia, radius and ulna were bowed; the circulatory system was normal; the Wassermann test was negative. He died from uremia ten days after admission to the hospital. At necropsy, both kidneys were found to be small and to have marked fibrotic changes. The histologic study of the bones was described in detail. In the roentgenograms general osteoporosis was found; multiple fractures and a characteristic stippled appearance were also present.

The third case was that of a girl 7½ years of age. The family history was negative. The patient had been a seven months' premature infant and was breast fed for six weeks, after which she thrived on cow's milk; she had never walked. On examination, she was found to be 34 inches (86 cm.) in height; her head was square and bossed; the radius and ulna on both sides showed enlargement and deformity in the ends, giving the impression of old fractures; the chest was narrow and pigeon-shaped and the ribs were beaded; the legs were deformed, and genu valgum was present; the child was mentally backward and seldom talked; the urine contained albumin but no casts; the Wassermann reaction was negative. An attempt was made to correct her deformities, and shortly thereafter she died from uremia. At necropsy, the kidney was found to have great increase of fibrous tissue and a tendency to cyst formation. The roentgenograms and the histologic pictures in the bones were the same as in the second case. Paterson stated that in the sections of the bone there was an active development of abnormal tissue, but that there was almost complete failure in one essential element of the osteogenetic process, namely, the deposit of lime salts in the trabeculae.

Barber,[94] under the title of "The Bone Deformities of Renal Dwarfism," reported three cases of renal rickets, apparently not previously recorded by him. The first case was that of a boy 12½ years of age. He had had polyuria and polydipsia; his height was 48½ inches (123.2 cm.); his heart and arteries were normal; his systolic blood pressure was 100; his urine had a specific gravity of 1.006, a small amount of albumin was present and the daily quantity was 41 ounces (1,212.9 cc.); there were no deformities present. Three and a half years

later he again came under observation with a history that three months previously he had been in bed for four weeks because of an attack of influenza. Following this, his legs became crooked. At examination, he was found to be only 52 inches (132.1 cm.) in height; the knees and wrists were enlarged, and there was genu valgum; urinalysis was the same as already noted; the Wassermann reaction was negative. A roentgenogram of the wrist showed irregular calcification and the picture of rickets.

The second case occurred in a girl 13¾ years of age who had always been small. She walked when 2 years of age; her development had been poor since she was 6 years of age; she had suffered from thirst all her life; there had never been scarlet fever or any other serious illness. Her legs became crooked when she was about 13 years of age. On examination, she was found to be dwarfed (height, 45 inches [114.3 cm.]); there was marked genu valgum; the knees, wrists and costochondral junctions were enlarged; the urine showed a mild albuminuria, a specific gravity of 1.004 and a total daily quantity of 40 ounces; the heart and arteries were normal; the systolic blood pressure was 90; the Wassermann reaction was positive on two occasions; there was roentgenologic evidences of rickets. The family history was of no significance. The patient later died from uremia, and at necropsy, well marked interstitial nephritis was found microscopically. The age at death was not stated.

The third case was that of a girl 13 years of age who had genu valgum that had developed sixteen months before. When 3 years of age she had a condition that had been diagnosed diabetes insipidus, and at that time her urine had a specific gravity of from 1.008 to 1.010, and albumin was not found. After this she had an attack of scarlet fever. She had also had measles (age not stated). She had always been thirsty. She had weak legs. In her family history it was noted that one brother had died of heart disease. On examination, in addition to the genu valgum, her height was found to be 52 inches (127 cm.); pubic hair was present; in repeated examinations of the urine a trace of albumin was found, and the daily quantity was about 50 ounces (1,478.7 cc.); systolic blood pressure was 100; the Wassermann reaction was negative; the cardiovascular system was normal.

Taylor[48] reported two cases of chronic interstitial nephritis, in one of which changes of the bone were present. The case of renal rickets occurred in a boy whose age was not stated. There had been another child in this family in whom polyuria had developed at the age of 6 months, and who had died at the age of 3 years of Bright's disease. The patient was said to have been healthy until he was weaned at 14 months of age. At that time he had tonsillitis with fever for two and one-half weeks, and his parents dated his illness from that time. On examination, there was found marked rickets with genu valgum; about 2 liters of fluid were taken a day; the output of urine was large, but the exact amount could not be determined. It contained a trace of albumin and a few casts, and its specific gravity varied from 1.008 to 1.010; the two hour phenolsulphonphthalein excretion varied from 10 to 15 per cent; the blood urea nitrogen was 16.6 mg. per hundred cubic centimeters; the Wassermann reaction of the blood was negative.

Page[208] reported a case of renal dwarfism in a girl 7½ years of age who had clinical and roentgenologic evidence of rickets. Her urine usually contained albumin; functional tests showed kidney insufficiency, and there was increased blood urea.

Barber[118] gave a synopsis of three cases of renal rickets not previously reported by him. The first was that of a girl 20 years of age who was still alive at the time of the report. She was 12 inches (30.4 cm.) below the average height;

she had genu valgum which had developed at about 17½ years of age; her urine had a specific gravity of 1.006 and albumin was present; her systolic blood pressure was 110; her radial arteries were normal, but the brachial and femoral arteries appeared to be a little thickened; in the roentgenograms little change was noted "as the epiphyses were united." She had always been delicate; she had not had scarlet fever but after measles, at 4 years of age, she seemed to fail in health; menstruation began at 18 years of age; her sexual development was fairly normal.

The second case was that of a boy 15 years of age who had always been small and delicate. He had had thirst since 6 or 7 years of age; his urine had a specific gravity of from 1.005 to 1.010 with albumin constantly present and a daily quantity of 50 ounces; the roentgenograms "showed changes in wrists and ankles." He died shortly thereafter from uremia. There was no history of scarlet fever, but measles had occurred at 4 years of age.

The third case occurred in a girl 11 years of age who had always been small; she had had thirst since she was a baby; genu valgum had developed recently; the urine had a specific gravity of 1.005 and contained albumin; she died from uremia twelve days after admission to the hospital; at necropsy, the kidneys showed changes typical of chronic interstitial nephritis, the other organs being normal. There was no history of acute infectious diseases in this patient.

Peterson[17] reported a case of renal dwarfism in a girl 4½ years of age with changes in the bones. She had been a full term child; at birth it was noticed that her hands and feet were deformed by a twisting at the wrists and ankles. Her weight at birth was 5 pounds (2,300 Gm.); she was fed on breast milk until she was 1 year of age; she talked at 18 months of age; she sat up at 2 years, but never attempted to stand. The only illness was measles at 3½ years of age. The family history was without significance. On examination, the child was found to be very pale. She was 22 inches (25.4 cm.) in height; she had a large head and her fontanel was open; her intelligence was that of a 2 year old child; she had only seven teeth; there was marked beading of the ribs and a Harrison's groove; the radial artery seemed thickened; there was no hypertrophy of the heart, the systolic blood pressure was 95; the blood urea was 108 mg. per hundred cubic centimeters; the urine had a specific gravity of from 1.006 to 1.008, contained a cloud of albumin and a few red blood cells and pus cells; there seemed to be polyuria; the Wassermann reaction was negative; there were marked deformities of the extremities; in the roentgenograms marked osteoporosis, faint stippling and enlargement of the lower end of the radius and ulnar and separation of the epiphysis of the knee joint were found.

Veiling and Holyoak[209] described the case of a boy 12½ years of age. He had had pertussis at 4 years of age, after which his sight became worse and his legs crooked. On examination, his height was found to be 43½ inches (110.5 cm.) and his weight 3 stone 13 pounds 8 ounces (55 pounds, 8 ounces [25,980 Gm.]); his mental state was normal; he had primary optic atrophy in the left eye; his urine varied in amount from 26 to 40 ounces (769 to 1,182.9 c.c.) in twenty-four hours, and it contained a small amount of albumin and a few hyaline and granular casts; there were no definite cardiovascular changes; the systolic blood pressure was 95 and the diastolic 70; the Wassermann reaction of the blood was negative; in the roentgenogram of the sella turcica there was no definite abnormality, except that it was small and ill developed.

Shipley, Park, McCollum and Simmonds[139] reported the case of a renal dwarf 3½ years of age whose rachitic deformities were extreme; the roentgenologic and histologic bone changes were marked and differed from those ordinarily found in rickets; the specific gravity of the urine was low and appeared to be fixed, and

albumin was constantly present; several attacks similar to those of uremic acidosis occurred; the kidneys were found to be exceedingly small and defectively developed.

Greene [60] reported the case of a girl 3½ years of age who had bilateral hypoplastic cystic kidneys and in whom the clinical signs simulated chronic diffuse nephritis of congenital origin. The family history was unimportant, and there was no history of nephritis in any of the immediate relatives. The child had been born at full term, weighing 5 pounds; she was breast fed for a short time and after that was fed on cow's milk until the age of 8 months; her first teeth appeared at 1 year of age and she sat alone at this time, but she had never walked; at 8 months of age she had several convulsions followed by pneumonia, and when she was 2 years of age there was a similar illness accompanied by several convulsions. For several months before admission to the hospital she had been treated for a marked degree of rickets and received cod liver oil, phosphorus and iron. She did not eat well and it was also noted that her urine contained albumin but no casts. She was admitted to the hospital about three months before death, when her age was 3½ years, and at that time examination showed: marked underdevelopment (weight 22 pounds [10,000 Gm.]); an ivory-like pallor; extreme rachitic deformities of the head, chest and extremities; secondary anemia; albuminuria; 7 per cent phenolsulphonphthalein excretion in two hours; a total daily excretion of urine of 660 cc. with a specific gravity of 1.010, the latter having a tendency toward fixation. During the time the patient was in the hospital a number of other observations were made. She was bright and alert; she continued to have polyuria and polydipsia; her appetite was poor as a rule; the phenolsulphonphthalein excretion was low, varying from 4 to 10 per cent in two hours; there was always a slight albuminuria but never cylinduria; cultures of the urine were negative; the carbon dioxide capacity of the blood varied from 18 to 41 per cent by volume; at times she had hyperpnea; the nonprotein nitrogen of the blood was 48 mg. per hundred cubic centimeters; the Wassermann and tuberculin tests were negative; there was no albuminuric retinitis; her systolic blood pressure varied between 96 and 108 and the diastolic between 60 and 70; the kidneys were not palpable, and on cystoscopic examination a normal bladder was found; the liver and spleen were enlarged. Before death, vomiting and anuria developed. At necropsy, the heart and the suprarenals were found to be normal; the bladder had no abnormalities; the ureters were somewhat dilated, but there were no strictures; the kidneys were atrophic, and the pathologic picture was that of hypoplasia with cystlike dilatations of the tubules, and signs of chronic inflammation, for the most part interstitial, were present.

Greene stated that the functional insufficiency rather than the pathologic changes in the kidney determined the clinical picture.

Greene [78] gave a good review of the literature and a discussion of chronic diffuse nephritis in children. The case he reported was that of a 4 year old girl who had had frequent attacks of bronchitis but who had not had measles, scarlet fever or any other contagious disease. Her complaints were nervousness, convulsions and vomiting. The only clinical evidence of rickets was moderate beading of the ribs; no roentgenograms were made. There was haziness of the optic disks. The bicarbonate capacity of the blood serum was 14 per cent by volume. At necropsy, marked evidence of chronic nephritis was found.

Evans,[121] in a study of arteriosclerosis in children, reported three cases not elsewhere recorded. The first of these occurred in a boy 14 years of age who had bone changes. His family history was without significance; he had been breast fed for eleven months; he walked and talked at the usual age; he had had measles at 4 years of age, bronchopneumonia at 5 years and tuberculous gland-

in the neck at 8 years; he had had bronchitis every winter but no history of scarlet fever, rheumatism or convulsions. At 7 years of age he had been operated on for genu valgum following which he had a convulsion. At that time the patient's weight was 2 stone, 12½ pounds (40½ pounds [18,300 Gm.]) and the height 38¼ inches (95.2 cm.); the systolic blood pressure was 195 to 170; the urine had a specific gravity of 1.023 or less and contained a small trace of albumin and epithelial casts, 30 ounces (887.2 cc.) being passed in twenty-four hours; renal efficiency tests showed that the excretion of sodium chloride, potassium iodide and lactose were normal, but there was a great rise in excretion of water, these things being taken to mean that the patient's "cardiovascular apparatus and glomeruli were disorganized;" the optic disks were normal. After his discharge from the hospital, the boy remained in his usual health until 13 years of age, when he began to have headaches and failing vision, but there was no history of edema, frequency of micturition or hematuria. When examined at 14 years of age, he was found to have marked clinical and roentgenologic evidence of rickets, marked cardiac hypertrophy, thickening of the radial artery, suggestive clinical signs of aneurysm of the aorta and roentgenologic evidence of a dilated one, a systolic blood pressure of 260 and a diastolic of 200, albuminuric retinitis and retinal hemorrhages, albuminuria and cylinduria, a daily urinary excretion of 45 ounces (1,331.2 cc.). He had no edema or signs of syphilis, and the Wassermann reaction of the blood was negative. He died three months later after a convulsion followed by coma and the signs of cerebral hemorrhage. At necropsy, there were found cerebral hemorrhage, cardiac hypertrophy (left ventricle), arteriosclerosis, chronic nephritis, normal ureters and bladder. In the kidneys there appeared to be a congenital reduction in substance, there being only two well formed pyramids; the renal arteries showed arteriosclerosis; the amount of interstitial change was relatively slight.

Watson-Wemyss [201] reported a case of chronic interstitial nephritis in a girl 9 years of age who had rickets. Her family history was unimportant. She seemed healthy until 2 years of age, but had never been strong since then, and at that time she began to show marked evidence of rickets. She had diphtheria at 3 years of age; at 4 years a double osteotomy was performed for genu varum. She was also said to have had whooping cough, pleurisy, bronchitis and a cellulitis of the leg. Six months before admission to the hospital, she began to have headaches and vomiting. On examination, she was found to be undersized and stunted, and her weight was 39 pounds (17,700 Gm.); her height was 42 inches (106.6 cm.); she was pale; her intellectual development was that of a child of 6 years of age; her heart was enlarged, and the second aortic sound was accentuated; the peripheral blood vessels were readily palpable; the systolic blood pressure was 204; there was an albuminuric retinitis; the urine had a specific gravity of 1.014 and contained albumin but no casts (before death, blood appeared in the urine); the quantity was rather small; the nonprotein nitrogen of the blood was 36 mg. per hundred cubic centimeters and the urea nitrogen 15.3. She had several convulsions; on several occasions she had carpopedal spasm. Later, her blood pressure increased to 240. Facial paralysis developed following one of the convulsions, and the patient died when about 10 years and 2 months of age. At necropsy, chronic interstitial nephritis was found; the left ventricular wall was hypertrophied; the aorta showed a marked nodular atheromatous change. The suprarenals were distinctly enlarged and congested, but no particular abnormality was found on microscopic examination.

Ogilvie [10] reported a case of renal rickets in a boy, aged 17 years, who had always been considered small, but who had learned to walk and talk at the usual

time, had been physically active and mentally alert. About the age of 15 years he began to have stiffness in his knees. When 16 years of age he sprained his ankle and had not walked without assistance since that time. Nocturnal enuresis had been a symptom until the past year. He was small (appearance of a boy of 12 years); his external genitalia were well developed but pubic hair was scanty and the voice childish; the head was square; there was obvious enlargement of the epiphyses of the wrists and ankles and marked genu valgum; the blood pressure was 122 systolic and 70 diastolic; the urine was alkaline, contained pus and triple phosphate crystals, albumin and *Bacillus coli* in large numbers, its specific gravity being 1.009; the blood urea was 270 mg. per hundred cubic centimeters; the Wassermann reaction was negative. In the roentgenograms all epiphyseal spaces were found wide and ragged in outline, but there was no cupping of the diaphyses and no evidence of renal calculi.

Roth[140] reported a case of renal rickets in a girl 13 years of age. She was small, sallow and had extreme genu valgum. "The urine was characteristic (pale, specific gravity, 1.005, albumin one-half on boiling and standing)." In the roentgenograms, the internal condyles were found to be enlarged; there was spongy-looking transparent bone and patches here and there in the diaphysis where the bone appeared almost missing; according to the urea concentration test, there was marked kidney insufficiency. Double supracondylar osteotomy was performed under gas and oxygen anesthesia with no untoward result.

Kendall[55] reported a case of renal rickets in a girl 4½ years of age who had been well until 2½ years of age when general edema, diarrhea and vomiting suddenly developed. These symptoms recurred during a period of four and one-half months, but on repeated examination albuminuria was not found. The Wasserman reactions of the patient and her mother were positive, but the father's reaction was negative. She was discharged from the hospital but was readmitted when about 4½ years of age with the history that the attacks of edema, vomiting and diarrhea had continued; that when about 4 years of age knock-knees developed; that since 3½ years she had been drinking rather large quantities of fluid and at times had had polyuria. She was found to weigh 32½ pounds (14,750 Gm.) and to be 36 inches (91.4 cm.) in height; she appeared intelligent; there was edema, carpopedal spasm, a positive Chvostek sign, albuminuria but no cylinduria; the cardiovascular system was normal; the systolic blood pressure was 85 and the diastolic 55; the fundus in each eye was normal; the blood urea was normal; genu valgum and enlargement of the lower ends of the radius and ulna were noted; roentgenologic study showed translucency and striation of the ends of the diaphyses of the tibia and femur, translucency and irregularity but no striation of the ends of the diaphyses of the radius and ulna and some periosteal thickening of the shafts. The Wassermann reaction at this time was negative.

The author was not sure that this was a case of renal dwarfism, but he did not seem to think that congenital syphilis was responsible for the symptoms. Several who discussed the case thought that the condition was due to intestinal disease because of the definite history of diarrhea; in other words, this may have been an instance of celiac infantilism.

Still,[28] in his book, cited eleven cases of chronic interstitial nephritis which he had seen in children. Two of these were brothers who had changes of the bone. The younger was 5 years and 7 months of age. He had not walked until he was 3½ years old, and at that time had knock-knees which gradually became more marked. His height was only 34¾ inches (87.8 cm.). He had frequency of micturition and great thirst; his urine was pale and contained a heavy cloud of albumin; on certain tests (the nature of which are not described) his renal

function was found to be very deficient. The elder was 6 years and 1 month of age; he had had knock-knees since the age of 2½ years; his height was only 35½ inches (90.1 cm.); his urine was pale with a specific gravity as low as 1.004; a slight cloud of albumin was present, and the urea concentration test showed that renal function was deficient. In both these children the Wassermann tests were negative. A picture of the children is in Still's book, and the statement is made that the cases were those of Mr. H. A. T. Fairbank.

Baar[199] reported a case of renal rickets in a girl 14 years of age. At 2 years of age she had cystitis; she had not been well since that time and had suffered from weakness and fatigue. For two months before admission she was bedridden; she became quite pale and had edema of the face, nosebleed, headache and vomiting. On examination, she was found to have severe rickets and genu valgum and flat feet; she was anemic in appearance; she had edema of the face and legs; there was ecchymosis of the mucous membranes of the mouth; the heart was enlarged to the left; a marked secondary anemia was found; the nonprotein nitrogen of the blood was 105 mg. per hundred cubic centimeters; the daily quantity of urine was between 700 and 1,900 cc., its specific gravity between 1.007 and 1.012; albumin was present and many leukocytes but no casts; streptococci were also found but no colon bacilli; there was fixation of the specific gravity of the urine; there was no sclerosis of the peripheral vessels. Baar did not think that the chronic interstitial nephritis in this case was secondary to arteriosclerosis or an ascending pyelonephritis.

Ashcroft[30] stated that in 1921, two rachitic persons died from uremia in Ancoats Hospital, and that since 1922, all persons with rachitic deformity who were thought to be suffering from renal disease were examined for evidence of it. Of twenty-four such patients, eight were found to have definite signs of renal insufficiency (inefficiency). At necropsy, chronic interstitial nephritis was found in three cases. Among other things noted were thickening of the capsule and increase in the connective tissue of the suprarenal glands and altered staining reactions in the zona reticularis, which led Ashcroft to suggest that these alterations meant deficient secretion and had etiologic significance. One of the cases, that of a girl 18 years of age, was described in some detail. She had had bowing of the legs since the age of 4 years; growth had ceased at 15 years; there was no beading of the ribs; the teeth were "poor;" there was enlargement of the epiphyses. The patient had clinical evidence of nephritis, and in the roentgenograms the changes of rickets were discovered. (For description of roentgenograms see section on pathogenesis.)

Barber[138] stated that he had seen seven more cases of renal dwarfism since the ten he collected in 1921.[113] Eight postmortem examinations had revealed in each instance small kidneys with pure chronic interstitial nephritis. Only three of these seventeen patients died without obvious deformities of the bone. He noted that bilateral cystic disease of the kidneys and calculi in both kidneys may give rise to a urine similar to that in chronic interstitial nephritis, and quoted Dr. Cameron as having mentioned a case in which the latter condition caused renal dwarfism. (In the paper by Cameron[137] this case is not mentioned.) No quotation is given by the author of the case caused by congenital cystic kidneys. Apparently two cases are reported in this paper which Barber had not previously described. The first of these was that of a girl still alive at 19 years of age who was much under the average size and who had had genu valgum for six years. She had a blood urea of 164 mg. per hundred cubic centimeters; a systolic blood pressure of 120 and a diastolic pressure of 75. In the roentgenograms, the bones were found to be less dense than normal. She had menstruated regularly for two

years. (This case may possibly have been included in a previous report.) The second case was that of a girl 12½ years of age who had had genu valgum for three years. She had had polydipsia for a long time. In the roentgenograms, delay in ossification was found; the blood urea was 113 mg. per hundred cubic centimeters; the systolic blood pressure was 100 and the diastolic 85.

Lathrop[114] reported a case of renal rickets in a girl 15 years of age whose family history was unimportant; she had had pertussis at 8 months of age, smallpox at 5 years, influenza at 9, typhoid at 11 and mumps at 13; she had not had scarlet fever, diphtheria or tonsillitis; she had never been strong but had seemed to develop normally until after the attack of typhoid fever, since which time there had been distinct retardation of physical growth; she had developed normally mentally, but had not menstruated. From the age of 12 years she had shown fatigability, lack of energy and drowsiness, and about that time albumin was found in her urine, and later casts and a low specific gravity were noted. In a hospital it was also discovered that her blood pressure was 110 systolic and 70 diastolic; the phenolsulphonphthalein output was 11 per cent (in two hours?) and the nonprotein nitrogen of her blood 74 mg. per hundred cubic centimeters. During the next two and one-half years she was admitted to the hospital five times. Headaches, nausea and vomiting developed, and at about 13 years of age, and rather suddenly, genu valgum appeared. At 14½ years of age she began to have palpitation, dyspnea and slight edema of the eyelids and feet. About this time polydipsia, polyuria and anorexia were noted. When examined at 15 years of age, she was 58½ inches (140.4 cm.) in height, and 73¼ pounds (33,300 Gm.) in weight; the systolic blood pressure was 100 and the diastolic 60; her intelligence was good; her nourishment was good, but her development was poor, the breasts being small and the secondary sexual characteristics absent; her skin was dry and her color pasty, and it later became brownish; she had marked genu valgum, enlarged costochondral junctions and wrists; there was no evidence of disease in her eyegrounds; her heart was normal; she had a secondary anemia; her urine had a specific gravity of from 1.005 to 1.010 and contained small amounts of albumin, many pus cells but no casts, and there was fixation of specific gravity; the Wassermann reaction was negative; the roentgenograms showed a marked retardation of development of the epiphyses, especially of the wrists; the blood pressure varied from 90 to 150 systolic and was usually about 80 diastolic; the nonprotein nitrogen of the blood varied from 100 to 244 mg. per hundred cubic centimeters; the blood calcium varied from 4.6 to 5.9 mg. per hundred cubic centimeters, the phosphates from 9.1 to 9.5, the free calcium was 3.8, the carbon dioxide capacity varied from 18.9 to 33.2 per cent by volume. She died at the age of 15 years and 1 month. At necropsy, the heart and blood vessels appeared normal, but there was fine scarring of the myocardium on microscopic examination; the bones had irregular lines of ossification and broad zones of connective tissue in which islands of osteoid tissue were embedded; the kidneys were distorted, small and firm and showed striking microscopic changes which consisted of scarring and complete distortion of the normal kidney architecture and extreme reduction of kidney substance, the tubules being enormously dilated. There was little disease of the blood vessels. There was evidence of a chronic cystitis and pyelitis. The suprarenals were normal.

Wyllie[126] reported a case of renal rickets in a girl 11 years of age. She had been an eight months' premature infant. She was the youngest of ten children, the others being healthy. She was late in walking; she had always been thirsty and had had enuresis, but had never had headaches. On examination, she was found to be much undersized (43¼ inches [110.4 cm.] in height and 45 pounds

[20,400 Gm.] in weight); she had a sallow skin, genu valgum, enlarged epiphyses and beading of the ribs; the heart was normal; the optic fundi were normal; the systolic blood pressure was 110, the diastolic 80; there were polydipsia and polyuria; the urine had a specific gravity of 1.010, contained albumin but no casts; there was lack of ability of the kidneys to concentrate urea; the blood urea was 171.6 mg. per hundred cubic centimeters.

Parsons,[81] in his last publication, included five hitherto unreported cases of renal infantilism with changes of the bone. One of these occurred in a boy still living at the age of 17 years who had a marked rosary, enlarged epiphyses and great deformity of the bones of the arms and legs. The ages and description of the other patients are not given. In all his cases, genu valgum developed before the patient was 10 years of age. His description of clinical and roentgenologic characteristics are clear and his discussion of pathogenesis is interesting. He found that there might be extreme lipemia; that in all cases there was a high degree of nitrogen retention; that the blood phosphorus was greatly increased (varying from 4.1 to 16.13 mg. per hundred cubic centimeters of inorganic phosphorus); that the serum calcium varied from 3.95 to 14.6 mg. per hundred cubic centimeters but that, while in only six of twenty-one estimations was the calcium below 9 mg., it was low in every patient when compared to phosphorus; that there was a tendency to acidosis (low carbon dioxide, increased hydrogen ion concentration). Parsons believed that there is an inability of the kidney properly to excrete phosphate; that is, that a true endogenous rickets exists. The blood calcium, while low when compared to blood phosphorus, frequently had normal values in contradistinction to what usually obtained in azotemic nephritis and after the injection of phosphates. The suggestion is made that this is due to mobilization of calcium from the bones as a preventive mechanism against tetany. Parsons thought, too, that ultraviolet irradiation aggravates the bone changes. He stated that in the great majority of cases necropsy has shown very small kidneys, the result of chronic interstitial nephritis, but cases are on record associated with pyelitis and apparently an ascending infection of the urinary tract, congenital cystic kidneys and bilateral renal calculi. The end-result is, however, identical in all cases, that is, an almost complete destruction of the renal parenchyma.

Brockman[147] reported three cases of chronic interstitial nephritis and renal rickets in children, in two of which the diagnosis was made from clinical observation, blood urea examination and roentgenograms, and apparently the condition followed attacks of acute nephritis. The first case was that of a boy 14 years of age who when 2½ years old suffered from an attack of acute nephritis. Until 7 years of age he had frequent attacks of vomiting; when 13 years of age genu valgum began to develop and subsequently became marked; he passed from 50 to 60 ounces of urine daily; his blood urea was 102 mg. per hundred cubic centimeters; he was alive at the time of the report.

The second case was that of a girl 11 years of age who when 3 years of age had an attack of acute nephritis which developed into a chronic condition. At 8 years of age she began to develop genu valgum. Her blood urea was as high as 162 mg. per hundred cubic centimeters before death in uremia.

The third case was that of a boy 13 months of age who was admitted to the hospital for treatment for rickets. He had vomited frequently; he had not grown since 6 months of age; he was small; he had marked deformities of the upper and lower limbs, the hands being radially adducted and the feet twisted upward; there was beading of the ribs and enlargement of the epiphyses of the wrists and ankles; in the roentgenograms osteoporosis, "splaying out" of the lower ends of the radius, ulna and tibia, and epiphyseal dislocation were found. At necropsy,

congenital cystic disease of the kidneys was discovered and on histologic examination the changes of chronic interstitial nephritis.

Smith and Walsh[142] gave details of a case of renal rickets in a boy studied at the age of 14 years whose illness and symptoms followed pneumonia developing after pertussis at 10 years of age. It was stated, however, that the patient had no evidence of renal disease at that time. He died at the age of 15 years and 5 months from uremia, and no necropsy was obtained. He had the roentgenologic evidence of late rickets and osteomalacia; there were anemia and marked stunting of growth; he was mentally alert; there was no pubic hair, and the genitalia were underdeveloped; he had polyuria and polydipsia; the Wassermann reaction and the tuberculin skin reaction were negative; the urine was large in amount, albumin was present, and the phenolsulphonphthalein excretion was less than 10 per cent in two hours; the blood calcium was 5 mg. per hundred cubic centimeters and the inorganic phosphorus 5.6; there was nitrogen retention.

Hunt,[6] in his paper on renal infantilism with a review of the literature, reported the case of a girl 3 years of age on whom the clinical diagnosis of chronic interstitial nephritis and renal rickets was made. One of the paternal grandparents had died from chronic interstitial nephritis, and during gestation the mother was ill with vomiting, epigastric pain and transient amaurosis. According to the family physician, however, she at no time had an elevation of blood pressure or albuminuria. The infant was normal at birth. Eruption of teeth was slow, only ten being present at 3 years of age. Growth was slow, and the child could never stand or walk without support. At 2 weeks of age vomiting began which might have been due to a pylorospasm. There were no symptoms of tetany. Polydipsia began at about 1 year of age, and there was marked anorexia. At about 2 years of age polyuria was noticed, and about this same time deformity of the wrist began followed by deformities of the bones of the chest and extremities. These were treated with sunlight and ultraviolet light and cod liver oil. At about 3 years and 4 months of age, there was an attack of influenzal pneumonia complicated by edema and coma. On examination, the child appeared poorly developed; she was bright and alert; she weighed 16 pounds 13 ounces (7,626 Gm.) and she was 29 inches (73.6 cm.) in height; the skin was brownish, but the sclerae were clear; her mentality appeared normal; the anterior fontanel was widely open, and there was a rachitic rosary and a Harrison's groove; there were marked deformities of the bones of the upper and lower extremities and the chest and enlargement of the epiphyses; the heart was normal; the kidneys were not palpable; there was no retinitis; the urine had a specific gravity of 1.008, and there was a trace of albumin but no casts; the serum calcium was 9.6 mg. per hundred cubic centimeters, the serum phosphorus 7.5; the total nonprotein nitrogen of the blood was 107 mg., the creatinine 5.4, the uric acid 8.9, the sugar 76; the phenolsulphonphthalein excretion was 3 per cent in two hours; on roentgenologic examination of the long bones there was found a general medullary rarefaction with acute, rachitic-like epiphyseal changes and periosteal thickening; the systolic blood pressure was 138 and the diastolic 72; the Wassermann test of the blood was negative; the tuberculin skin test was negative; under observation polyuria and polydipsia were marked. The patient was readmitted when about 3 years and 2 months of age, when the examination was practically the same as on the previous admission. The child died two weeks later after having convulsions followed by coma.

Karshner[98] reported a case of renal rickets in a girl 7½ years of age. Her father had a 4 plus Wassermann reaction. She walked at 3½ years of age; she had a fracture of the femur at 2 years and 9 months; her first tooth appeared at

the normal time, but decayed rapidly; she had had a proper diet and exposure to the sun; there was a history suggestive of tetany; she had had polyuria and polydipsia for years; she was undersized, had carious teeth, beading of the ribs, enlarged epiphyses, bowed legs and genu valgum; the urine had a specific gravity of 1.010, contained much albumin as well as casts and red blood cells, and on one occasion only was copper reduced; roentgenograms showed the picture of active rickets without healing; the Wassermann reaction was not reported; the blood calcium was 8 mg. per hundred cubic centimeters and the phosphorus 4; the systolic blood pressure was 180 and the diastolic 80. At necropsy at 9 years of age, chronic interstitial nephritis, dilatation of the heart and, among other conditions, atheroma of the aorta and endocardium were discovered.

Apert [202] reported the case of an undersized boy 4 years of age with normal mentality who had clinical and roentgenologic evidence of rickets and at whose necropsy atrophic kidneys were found.

Cockayne [209] reported two cases in children which he classified as renal dwarfism. The first of these was that of a girl about 6 years of age who was small in height and weight and anemic. She had had no infectious diseases; she had had attacks of vomiting and two convulsions in the previous three months. Her urine contained albumin and was of a low specific gravity, the amount varying from 320 to 1,660 cc. daily. Roentgenograms of the wrist, shoulder, ankles, knees and hips were normal, but there was slight delay in ossification. There was nitrogen retention and the blood chlorides were from 510 to 610 mg. per hundred cubic centimeters. Uremia developed. The patient did not die and, according to Cockayne, the diagnosis was either congenital cystic kidney or renal dwarfism, against the former there being absence of clinical and roentgenologic evidence of enlarged kidneys and the early age of the development of uremia.

The second case of this author occurred in a boy 5 years of age who had had pneumonia at 1 year of age, and measles, whooping cough and influenza during his fourth year. He was small in height and weight; he had cardiac enlargement (?), but no thickening of the arteries and no retinitis; there was marked clinical evidence of rickets and genu valgum; roentgenograms showed widening and irregular ossification of lower ends of the radius and ulna; green-stick fractures and delay in the centers of ossification were found; there was blood nitrogen retention, and the blood chlorides were 515 mg. per hundred cubic centimeters. No necropsy was obtained when the patient died.

Scott-Easton and Paterson [146] presented a case of chronic interstitial nephritis with changes of the bone in a boy (one of twins) 4½ years of age who had failed to grow and who for at least a year had had polyuria and polydipsia. He weighed 23 pounds (10,400 Gm.); he was pale; his urine had a specific gravity of 1.001, contained a trace of albumin, many pus cells and *Bacillus coli* and the quantity was 30 to 40 ounces (887.2 to 6,182.9 cc.) daily; the heart was hypertrophied; the systolic blood pressure was 90; the radial vessels were palpable; the optic disks were normal; the roentgenograms showed osteoporosis but no sign of rickets. The patient was seen a year later, at which time he was circumcised because of a marked phimosis. At this time roentgenograms failed to show any changes in the bones. The Wassermann reaction was negative; his blood contained from 109.6 to 209.6 mg. per hundred cubic centimeters of urea, 146 mg. of cholesterol, 9.5 mg. of calcium and 25 mg. of phosphates. This case was regarded as one of interstitial nephritis accompanying pyelitis, and in the discussion it was stated that the malformation was probably congenital; possibly there were dilated ureters and hydronephrosis. The question was asked whether the phimosis could have caused back pressure and have been in any way responsible.

György [20] discussed the subject of renal rickets quite extensively. He included in his review some cases of renal infantilism not given by Hunt [8] and raised the number which he could collect to seventy-eight, including the fifty-four mentioned in Hunt's paper. He stated that while Fletcher thought it not unlikely that some type of urinary infection might produce interstitial nephritis after birth, no evidence was given to support this view. However, György had discovered four cases of renal dwarfism with or without rickets in which cystitis and pyelitis were present. These are the cases of Porter, of Lathrop, of Ogilvie (abstracted in another place in this paper) and of Kucerenko.[21a] The first case of renal rickets reported by György was that of a 10 year old girl. From the history, it is deduced that an attack of cystitis occurred about six years before the child was first seen. Some time after that polyuria and polydipsia developed, and about five years before pain in the knee and limping were noticed and knock-knee developed. Growth was stunted. Sunlight treatment had no effect. A fracture of the hip had followed a fall out of bed. The father was supposed to have had renal disease. On physical examination, the bone deformities were evident and in the roentgenograms osteoporosis and some rachitic alterations were found. The body was dwarfed, according to the measurements; the skin had a brownish pigmentation; the eyegrounds were normal; there was bilateral otitis media; a moderate anemia was present; the blood pressure was not elevated; a catheterized specimen of urine contained pus, and the culture contained *Bacillus coli* and staphylococci; the urine always had a low specific gravity, and the power to concentrate was poor; the nonprotein nitrogen of the blood was enormously elevated; on cystoscopic examination chronic cystitis was discovered, and it was said that a pyonephritis was indicated; indigo carmine excretion by the kidney was markedly diminished. It was stated that in this case there was increased blood phosphorus and decreased blood calcium, but the figures were not given. Marked clinical improvement and, according to the roentgenograms, bone healing occurred after the administration of viosterol, but in spite of seven months of such treatment there was not complete healing, and the blood chemical alterations did not become normal.

The second case occurred in a girl 10 years of age when first seen who had been treated without effect for several months for chronic colon bacillus pyuria. Three years later she returned with symptoms not present before. At this time she showed polyuria, knock-knees and retarded growth; there was increased blood pressure; the urine contained pus, albumin and colon bacilli, its specific gravity was low, and there was lack of power to concentrate; the serum calcium was 7.8 mg. per hundred cubic centimeters and the phosphorus 4.5 mg.; the nonprotein nitrogen was 50 mg.; on urologic examination chronic granular cystitis was found, and the pyelogram (made only on the right side) was normal.

Boone [57] reported a case of chronic diffuse nephritis in a girl who died at 3 years and 2 months of age. The paternal grandmother had chronic kidney trouble. The infant was normal at birth, but from the date of weaning there was difficulty in the feeding, and practically everything except milk was refused. At 1 year of age the weight was 16 pounds 12½ ounces (7,600 Gm.). The administration of cod liver oil was started at 7½ months of age. The child had had a few respiratory infections and an attack of pyelitis at 15 months of age. The first examination was made at the age of 19 months, and the complaints at that time were anorexia, vomiting and failure to gain in weight. These symptoms dated from about 9 months of age. When examined at that time the weight was 16 pounds (7,300 Gm.), the height 29 inches (73.4 cm.); development and nutrition were poor; the skin was pale; the patient was unable to stand; the mentality was below normal; the anterior fontanel was quite large; there were frontal and parietal

bossing and marked beading of the costochondral junctions as well as enlargement of the epiphyses of the long bones; ten teeth were present; the heart was normal; the urine contained albumin, but was negative microscopically. Under observation, the child gained slowly; a typical acidosis developed on one occasion; the fluid intake varied from 1,500 to 2,000 cc.; the nonprotein nitrogen of the blood was 47 mg. per hundred cubic centimeters, the creatinine 2.9 and the sugar 120; the systolic blood pressure varied from 100 to 120 and the diastolic from 60 to 68; the urine had a specific gravity of 1.004; on numerous occasions it contained a trace of albumin and occasionally a granular cast. Death occured in uremia. On necropsy, it was found that the heart was hypertrophied; the aorta and large vessels were normal; the kidney had undergone a general fibrotic change and had the microscopic appearance of chronic interstitial nephritis; the bladder and ureters were normal; the suprarenals were normal.

Kramer[152] stated that in a case of renal dwarfism he found the calcium and inorganic phosphorus of the blood both about 5 mg. per hundred cubic centimeters. In this case there was a transverse fracture of the tibia.

Schick[151] stated that he had under observation a patient 7 years of age who had always been pale and delicate and had polyuria and polydipsia. Bone deformities became marked at 5½ years of age; the urine had a low specific gravity with a lack of ability of the kidneys to concentrate the urine; the blood urea was 143 mg. per hundred cubic centimeters; the blood cholesterol was 518 mg.; the calcium varied from 10.6 to 11 and the phosphorus from 4.2 to 8 mg. Treatment with viosterol brought about some healing of the rickets.

Zanoli[145] reported two cases of renal rickets. The first was in a boy who came under observation when 16 years of age. The family history was unimportant. The boy had been born at full term; labor had been normal; he had been breast fed. He had never developed satisfactorily; he had progressed well in school; following infancy, he continued to have enuresis. He had not had any illness worthy of note. At about 6 months of age and without any apparent cause or local swelling or pain, left genu valgum slowly began to develop. On examination, he was found by actual measurement to be undersized; the nourishment was poor, but the muscular development good; there was pallor of the skin and mucous membranes; there was scarce growth of pubic hair and no axillary hair; the sexual organs were only moderately developed; double genu valgum was present; the Wassermann reaction was negative; the urine contained a trace of albumin and many pus cells; its specific gravity was 1.009. Under ether anesthesia, supracondylar osteotomy was performed. The postoperative course was normal. Three and a half years later the patient was again seen. In the interim he had had no particular illness but had polyuria. At this examination he was found still to be undeveloped and undernourished; there was definite evidence of delay in sexual development and lack of growth of body hair; the skin was dry and wrinkled and had a pallid earthy yellow color; the teeth were normally developed; the heart was not enlarged; the first sound was impure; the systolic blood pressure was 130 and the diastolic 80; flat feet were present; the genu valgum had remained satisfactorily corrected; nothing particularly abnormal was found in the roentgenograms of the bones; the daily quantity of urine was about 3,500 cc.; the specific gravity varied from 1.004 to 1.006, and it contained a trace of albumin and many pus cells; in the roentgenogram of the bladder a large calculus was found.

The second case occurred in a boy 17 years of age. The family and hereditary histories were without interest. The patient was born at full term; during pregnancy the mother had been much emaciated. The patient had never developed well; he had not had the usual exanthems. At 1½ years of age he began to have

pain in both knees, and about two months following this genu valgum developed. The only other important fact in the history is that as an infant he passed large amounts of urine. On examination and by actual measurement, he was found to be underdeveloped and undernourished; the musculature was hypotonic; the skin and mucous membranes were pallid, and there was a yellowish discoloration; there was delayed sexual development; the hairy growth of the body was scanty and the hair itself dry; there was no cardiac enlargement; the second pulmonic sound was accentuated, and there was a soft systolic murmur at the apex; the systolic blood pressure was 110 and the diastolic pressure 60; the usual clinical signs of rickets were absent except for the double genu valgum; the Wassermann reaction was negative; the daily quantity of urine was between 1,050 and 1,450 cc.; the specific gravity varied between 1.003 and 1.006, and a trace of albumin was found; the results of the microscopic examination were negative; in the roentgenograms were noted some decalcification and also rarefaction and trabeculation of the spine, the pelvic bones, the femurs and the bones of the feet and hands. Supracondylar osteotomy was performed, and the postoperative course was uneventful.

Zanoli has a table in his article in which thirty-four cases of renal infantilism are summarized, including the two of his own. In twenty-three of these, according to the table, there were changes in the bone. In one, the only bone deformity was flat feet and in another club feet. The latter case was not proved by necropsy to be one of chronic interstitial nephritis. All the cases cited by Zanoli in which there seems to be definite evidence that renal rickets was present have been abstracted in this article with the exception of one which he quotes from Elmslie (the only reference given being the year 1920). This particular case cannot be discovered in the literature, but it may be summarized here as follows: Male, aged 15 years; small in stature; having delayed puberty; having multiple bone deformities; having a trace of albumin in the urine. There is no notation of the termination of this case. These are all the data given in Zanoli's table.

Schoenthal and Burpee[148] reported a case of renal rickets in a boy 8 years of age. The family history was unimportant. The patient had been born at full term and was normal at birth; he was breast fed for three months and then put on supplemental feedings; he sat up at about 5½ months of age; his first tooth appeared at 11 months; he talked at 1 year; he walked at 16 months. His diet was always well balanced. He had whooping cough at 2 years of age and scarlet fever complicated by bilateral purulent otitis media at 3 years. He had always been pale; at 3 years of age he had clinical evidence of rickets; enuresis began at about the same time, and albumin was found in the urine. He was first examined when about 3½ years of age, when he had lobar pneumonia. At that time he had typical rachitic deformities, including genu valgum, and his urine had a heavy trace of albumin. The Wassermann and tuberculin tests were negative. He was seen again at 5 years of age, when the physical examination gave about the same results. His systolic blood pressure was 90 and his diastolic 60. There was an increased amount of phosphorus and urea in the blood, but the calcium and carbon dioxide were low. The urine had a low fixed specific gravity, and the phenolsulphonphthalein excretion was less than 10 per cent in two hours. Rachitic changes were demonstrated in the roentgenograms. His third admission to the hospital occurred at the age of 7½ years, and at this time he had convulsions. The situation was practically the same as on the second admission. At this time and at the time of a fourth admission shortly thereafter, metabolic studies were carried out. He had further convulsions and symptoms of uremia. The careful metabolic studies of this child are reported in the section on pathogenesis of renal rickets in

the present article. By personal communication it was learned that this patient died, and that at necropsy cystic kidneys were found.

R. P., a white boy, was admitted to the Children's Hospital of Cincinnati on March 11, 1929, when he was 18 months of age. The family history had no bearing on the case, the father and mother being alive and well, as were two brothers, and there was no history in the family of neoplastic, tuberculous, syphilitic, renal or cardiac disease. The patient had been born at full term by an instrumental delivery, following which he was cyanotic for a short time. He had been entirely breast fed for nine months and practically so for seventeen months. Orange juice had been given from 6 months of age, and practically nothing else had been added to the diet until cereals and green vegetables were offered at 1 year of age. Little cow's milk had been given until 17 months of age and cod liver oil not at at all. The first tooth erupted at 7 months of age, and the child walked at the age of 1 year. Since birth, he had had varying degrees of abdominal distention and constipation, which were somewhat relieved by cathartics. For several months he had vomited at frequent intervals. For an indefinite time, but for at least five months, it had been noticed that he had marked thirst and frequent urination. He had had no acute infections.

On the day before admission, he had been irritable and seemed to have fever; he had had a generalized convulsion accompanied by carpopedal spasm lasting for about five minutes.

On admission, it was found that the boy was apparently well nourished but undersized (17 pounds 14 ounces [8,000 Gm.]); his temperature was 98 F., his pulse rate 122 and respiratory rate 22. He appeared ill and cried frequently. Carpopedal spasm was present; Chvostek's facialis symptom was marked, and all reflexes were hyperactive. The anterior fontanel was closed; there was slight enlargement of the costochondral junctions and also of the wrists. The abdomen was markedly distended, making palpation difficult, but no masses could be felt by external or rectal examination. The liver was about 1 cm. below the costal margin, and the spleen could not be palpated. The eyegrounds were normal. The skin was not pigmented. There was no genu valgum. The rest of the physical examination revealed nothing abnormal.

It was found that the Wassermann and tuberculin tests were negative. A moderate secondary anemia was present without abnormality of red or white cells. In a large number of examinations of the urine it was noted that the specific gravity was always low (from 1.002 to 1.004), that albumin was occasionally present in small amounts, and that at times a large number of pus cells and a few red blood cells would appear. Large amounts of urine were passed, often more than 2,000 cc. a day, and the fluid intake was correspondingly great. The child would drink, if permitted, as much as 20 ounces (591.5 cc) or more within ten minutes. On one occasion, when put on a metabolism frame and the fluid intake restricted, he became quite toxic, and his temperature rose sharply, all symptoms disappearing when water was again given freely. The phenolsulphonphthalein excretion by the kidney was low, on one estimation about 15 per cent being eliminated in two hours and even less than this on another. The blood pressure was always elevated, ranging between 125 and 135 systolic and 95 to 105 diastolic. The blood chemistry is sufficiently important to be given in some detail (table 6).

In the roentgenograms of the bones there was marked evidence of rickets with cupping of the epiphyseal lines. Interestingly enough, a cystogram of the bladder was apparently normal with no filling of the ureters by the sodium bromide solution. It was not thought justifiable to give this patient a general anesthetic for the purpose of ureteral catheterization.

The patient remained in the hospital for three months from the admission on March 11, 1929. The abdominal distention was constant, and masses were never palpated. Polydipsia and polyuria were constant symptoms. The course was afebrile, except for the one occasion already mentioned. The general condition seemed quite good, and the child was alert mentally and as intelligent and as advanced in talking as the average child of his age (intelligence quotient not determined). Carpopedal spasm or convulsions did not return, although Chvostek's facialis symptom could always be elicited and constriction of the arm would be followed by the typical spasm of the hand. The diagnosis was renal rickets and renal infantilism. After discharge from the hospital, the boy was apparently in reasonably good health until about three days before readmission, when he contracted a mild infection of the upper respiratory tract and his urinary output diminished. Twelve hours before admission he became drowsy, and several hours

TABLE 6.—*Blood Chemistry in Patient R. P.*

Date	Plasma Inorganic Phosphorus, Mg. per 100 Cc.	Serum Calcium, Mg. per 100 Cc.	Urea, Mg. per 100 Cc.	Protein, Gm. per 100 Cc.	Nonprotein Nitrogen, Mg. per 100 Cc.	Carbon Dioxide per Cent by Volume
3/18/29	4.6	5.9	...	9.42 (plasma)	54	...
3/19/29	6.6	6.4	...	8.56 (serum)	...	...
3/30/29	7.9	6.7	...	...	...	...
4/ 4/29	6.8	6.8	...	...	...	...
5/ 8/29	6.4	7.5	...	8.40 (serum)	...	...
5/ 9/29	6.8	7.5	...	...	...	...
5/23/29	6.1	...	...	8.80 (serum)	60	...
6/ 6/29	...	...	93.8 creatinine (1.5)	...	...	...
6/18/29	5.2	7.0	...	...	...	...
10/ 1/29 (18 hours before death)	...	...	108	...	...	22 (serum); 10.7 (combining power)

later he began to have convulsions. At his entrance into the hospital he was in a typical uremic state, to which he succumbed about twenty-four hours later (aged 25 months). At necropsy, hydronephrosis of both kidneys with dilatation of all the remaining tubular structures was found. The ureters were enormously dilated and the bladder hypertrophied and dilated. There was fibrous change in the interstitial tissue of the kidney. Chronic inflammatory changes were present with increase of connective tissue of the submucosa of the membranous urethra, prostatic urethra and bladder. There was chronic inflammation of the submucosa of the ureters.

M. G., a white boy 11 years of age, was admitted to the Children's Hospital of Cincinnati on Nov. 11, 1928. His family history was without significance. When 3 years of age he had had pertussis and about the same time mumps; when 9 years of age he had had measles. Four months before admission he had a paronychia. He had been quite well and active until about three months before admission, when he began to vomit; three weeks before admission he had complained of headache and had five generalized convulsions in a period of two and a half hours. Following this he had nasal hemorrhage, tarry stools and purpuric skin manifestations.

and later a suppurative otitis media developed. A week before admission he began to have edema of the scrotum and feet. On examination, he appeared drowsy; he was poorly nourished; his color was pale and petechiae were present over his body; there was a discharge from both ears; there was no edema, except slight puffiness under his eyes; there was definite cardiac enlargement and accentuation of the second aortic sound; there was no clinical evidence of rickets, although roentgenologically there was some decreased density in the shafts of the long bones; several of his teeth were carious; his systolic blood pressure varied from 175 to 200 and his diastolic from 140 to 160; there was an albuminuric retinitis present; his bleeding and clotting time and the fragility of his red cells were normal, and he had secondary anemia; his urine contained a cloud of albumin and many hyaline and granular casts and a few red and white blood cells, its specific gravity varied

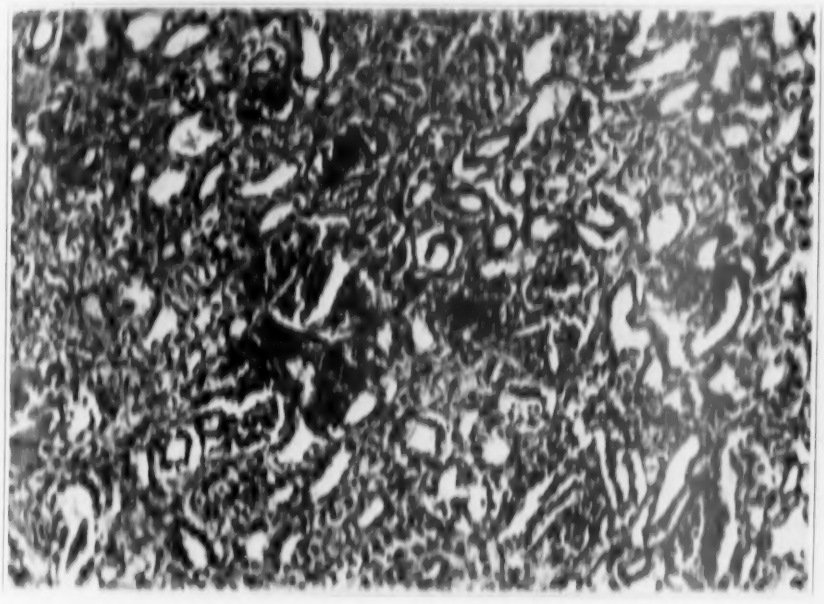

Fig. 2.—Section of kidney from patient R. P.

from 1.006 to 1.008, the daily quantity was as great as 1,500 cc. and there was fixation of specific gravity; the blood urea nitrogen varied from 12.5 to 75 mg. per hundred cubic centimeters; the Wassermann test was negative. The patient continued to vomit; he had no convulsions; he died about a month after admission. At necropsy, the kidneys were found to have advanced chronic arteriolar and arterial nephrosclerosis, there was some hydronephrosis on the right side, and both ureters and the bladder were hypertrophied and chronically inflamed. The left ventricle of the heart was hypertrophied; the aorta and coronary arteries showed no change. The suprarenals were normal.

APPENDIX

The following four cases of chronic nephritis are given in detail, because they have been included in the analysis in the present publication and because they are not elsewhere reported.

CASE 1.—J. A., a white boy, aged 7½ years, was admitted to the Children's Hospital in Cincinnati on Jan. 29, 1930. He had been a normal full term infant and in early life had had measles, mumps, chickenpox and whooping cough. He had been vaccinated against smallpox. At the age of 4 years he had pneumonia and had not been well since that time. Two years ago he had some edema of his feet which lasted a few days. For several years he had had polydipsia and polyuria. The patient's maternal grandmother had diabetes; his maternal grandfather died at 40 years of age from "dropsy" and heart disease; his paternal grandfather died at 36 years of age from kidney disease. Three months before admission his tonsils were removed, and at this time he had no albuminuria. One month before admission he began to have headache and vomiting, and three weeks before he had a number of convulsions over a period of two days. A week before admission he began to have swelling of his face, and at that time albuminuria was first discovered. The day before admission he complained of failure of vision and severe headache and became very drowsy. On examination, the patient appeared malnourished, and his weight was found to be 37 pounds (16,800 Gm.); his skin was pale and pasty; his heart was somewhat enlarged to the left and the second aortic sound was very loud; he had no clinical or roentgenologic evidence of rickets; the radial pulse was of high tension, but there was no palpable thickening; the systolic blood pressure was 170 and the diastolic 130; there was slight edema of the hands and feet; there was a marked bilateral retinitis; the nonprotein nitrogen of the blood varied from 35.7 to 39.5 mg. per hundred cubic centimeters; the serum calcium was 10.8 mg.; the blood phosphorus varied from 2.79 to 3.23 mg.; the urine had a specific gravity of 1.004, and it contained a moderate amount of albumin, a slight increase in the number of pus cells and occasional hyaline casts; large amounts were passed, as much as 2,400 cc. in twenty-four hours and the phenolsulphonphthalein excretion varied from 30 to 57.5 per cent in two hours; the Wassermann test of the blood and the intracutaneous tuberculin test were negative. Under observation, it was found that the results of urine examinations continued to be about the same as previously noted, and that the systolic blood pressure remained constantly elevated above 200. Ten days before death the boy developed convulsions, following which he became drowsy and died in coma. At necropsy, the kidneys were found to be of the chronic interstitial type with arteriosclerosis; the ureters were not dilated; there were atherosclerosis of the aorta and generalized arteriosclerosis; the left ventricle of the heart was hypertrophied; the suprarenals were normal.

CASE 2.—M. J. C., a white girl, aged 5½ years, was admitted to the Children's Hospital in Cincinnati. The family history revealed nothing of importance for anything in the nature of renal, cardiac or vascular disease. The patient had had measles at 1 year of age and whooping cough but no other diseases such as scarlet fever, diphtheria, chickenpox or mumps. She had always been delicate. She had been born at full term and weighed 7¾ pounds (3,900 Gm.). She was breast fed for two months; for two months more she had condensed milk and then cow's milk mixtures. Her appetite had always been poor. There had been no serious complaints until one month before admission, when the patient began to cough and have precordial pain, dyspnea and abdominal swelling. On examination, she was found markedly undernourished, the weight being only 28 pounds (12,700 Gm.); there was paleness but no discoloration of the skin; physical and roentgenologic evidence sufficient to warrant the diagnosis of a tumor of the lung were found; both kidneys were greatly enlarged to palpation; the radial artery appeared to be distinctly thickened and tortuous; the systolic blood pressure was 115 and the diastolic 80; there were no changes of the bone on clinical or roentgenologic

examination; the urine contained a considerable amount of albumin and many pus cells but no casts; the Wassermann test of the blood was negative as were also several intracutaneous tuberculin tests. Under observation, the masses in the region of the kidney became larger and then suddenly decreased in size so that they were no longer palpable. Later the masses became enormous in size and again disappeared, making the diagnosis of hydronephrosis obvious. The patient's condition never warranted ureteral catherization, but cystograms were made which were negative. The condition of the lung remained unchanged, except that its density decreased with roentgenologic treatment; bloody fluid was obtained several times on tapping the pleura, and this was sterile on culture, and guinea-pig inoculation was negative. The urine usually was low in specific gravity and albumin present in small amounts; pus cells were usually found in considerable number and occasionally hyaline and granular casts; the culture contained *Bacillus alkaligenes;* the phenolsulphonphthalein elimination in two hours was 50. The systolic blood pressure varied between 116 and 125 and the diastolic between 80 and 95. The nonprotein nitrogen varied between 28.7 and 150 mg. per hundred cubic centimeters, the urea nitrogen between 13.5 and 50, the creatinine between 2 and 4. The blood carbon dioxide was as low as 24 per cent by volume on one occasion. The inorganic phosphorus of the blood varied between 2.64 and 10.26 mg. per hundred cubic centimeters, the calcium between 9.9 and 12.2; the plasma chlorides were 100 mm. per liter. A severe generalized convulsion occurred following which increasing drowsiness developed, and the patient died without regaining consciousness. At necropsy, far advanced nephrosclerosis (chronic interstitial nephritis) was found. There was arteriolar and arterial sclerosis; a cerebral hemorrhage was present; there was a primary tumor of the thymus (thymoma) with metastasis to the kidney and suprarenal glands.

Case 3.—F. M., a white girl, aged 9 years, was admitted to the Children's Hospital in Cincinnati on Oct. 23, 1927, and is reported through the courtesy of Dr. J. S. Mathews. The family history was unimportant. The girl had had chickenpox and whooping cough and at 3 years of age pyelitis. When about 7½ years of age she had injections of toxin for the prevention of scarlet fever, and the parents dated her present illness from that time, but according to the history there were no active symptoms such as vomiting or headache until six months before admission. At that time albuminuria and high blood pressure were discovered, and a diagnosis of acute hemorrhagic nephritis was made. On examination, the patient was found to be pale and poorly developed and nourished (weight, 42 pounds [19,100 Gm.]); there was marked cardiac enlargement; there was no clinical evidence of rickets; the systolic blood pressure varied from 180 to 210 and the diastolic from 140 to 150; the eyegrounds had a marked retinitis and recent hemorrhages; the urine contained a cloud of albumin, many pus cells and a few casts, its specific gravity varied from 1.002 to 1.005, and the daily amount varied from 50 to 88 ounces (1,479.7 to 2,601 cc); the Wassermann test of the blood was negative; the urea nitrogen was 9.3 mg. per hundred cubic centimeters, the creatinine 2.5 mg. and the blood chlorides 440 mg. The patient had headache, vomiting and polydipsia while under observation. She died at the age of 10 years. She had no convulsions.

Case 4.—L. P., a girl, aged 11 years, was first admitted to the Cincinnati General Hospital on April 11, 1928. Two months previous to this time shortness of breath developed, which gradually became more marked. She became weak, complained of precordial pain which was worse on exertion and had a dry cough. She had been a full term, breast fed infant. At 8 years of age she had an attack of

acute nephritis accompanied by convulsions, following which she had never been quite well and had had nocturia. She had had measles, mumps, whooping cough and chickenpox, all of these diseases occurring before the nephritis. Her tonsils and adenoids had been removed at eight years of age. The family history was negative; the father and mother and three other children were alive and well, and there was no history of any chronic disease in the family. On examination, the patient was found to be poorly developed and nourished and acutely ill; she had marked dyspnea; her skin was pale; many of her teeth were carious; there was marked cardiac enlargement; the arteries were palpably thickened and hard; the liver was greatly enlarged; there was slight edema of the feet; the blood pressure was 178 systolic and 150 diastolic; the urea nitrogen of the blood was 75 mg. per hundred cubic centimeters, the uric acid 4.02 and the creatinine 2.03; the phenolsulphonphthalein excretion of the kidney was 12 per cent in two hours; the urine contained a trace of albumin, no casts but many pus cells; the tuberculin tests and the Wassermann test of the blood were negative; there was no clinical evidence of bone deformities; by clinical and roentgenologic study she appeared to have a chronic infection of her nasal sinuses.

She was admitted to the hospital three times until her death in uremia at 12 years of age. The course of the disease was varied. Edema appeared and disappeared as did also dyspnea and cyanosis. At one time blood appeared in the urine, and later many casts were found; there were always a trace of albumin and some pus cells. Polyuria and polydipsia were present; she sometimes voided as much as 2,300 cc. daily. The phenolsulphonphthalein excretion was diminished on several occasions. The blood pressure remained quite constantly elevated; the nitrogen retention in the blood varied; at times there was a distinct lowering of the carbon dioxide capacity of the blood (to 30 per cent by volume). A pasty yellow color developed. There were frequent attacks of vomiting and occasionally of headache. Stupor developed on several occasions, but no actual convulsions. No roentgenograms of the bones were taken, but there was no clinical evidence of rickets. On one examination of the eyegrounds no evidence of retinitis was found although later before death, at which time the eyes were not examined, there was dimness of vision.

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tinued, but there had been no edema for two years. He was markedly undersized. He had peg-shaped incisor teeth, and only two carpal osseous centers. There was no chloride retention. He had a high blood urea; a blood p_H of 7.28 and blood bicarbonate of 36.1. The blood pressure was elevated and there was hypertrophy of the heart. The Wassermann reaction was positive. The authors believed that congenital syphilis was responsible for both the infantilism and the chronic nephritis.

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plete study of the acids and base of the blood serum. He was able to show that the lowering of the bicarbonate was due to a deficiency of base in the serum and not to the presence of normal acids. Healing of the rickets occurred, the phosphorus slowly came down to normal and the calcium had higher values. This was not due to antirachitic treatment but to an improvement of renal excretion. This patient had had evidence of tetany.

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Pediatric Biographies

BENJAMIN RUSH

1745-1813

JOHN RUHRÄH, M.D.
BALTIMORE

In "Pediatrics of the Past," attention was called to the fact that no first rate biography of Benjamin Rush has been written, and this is the more curious since in the recent flood of biographies many men of far less merit and importance have been brought to the fore.

Benjamin Rush was born in Philadelphia County, Pa., on Dec. 24, 1745. Both his father and mother came from English dissenter stock, and in Rush the blood again ran true to form. His early schooling was in an academy in Nottingham, Md., conducted by the Reverend Samuel Finley who later became president of the College of New Jersey, now Princeton University, in which school young Rush continued his studies and from which he was graduated with an A. B. degree in 1760, before he was 15 years of age. Thence he went to live with Dr. John Redman in Philadelphia and was with him until July, 1766. During these six years he is said to have been away from work only eleven days and outside the house only three nights. That is the kind of a boy he was as a medical student, and that was the kind of man he grew into. His only other American medical education was two courses of lectures by Dr. Shippen and Dr. Morgan. He spent two years in Edinburgh, and received his degree in June, 1768, defending his thesis on the digestion of the food in the stomach. From Edinburgh he went to London, where he lived in the house with Benjamin Franklin, through whom he met many well known men of the day. He studied languages and could read French, Italian and Spanish as well as Latin. A short trip to Paris completed his European education, and on his return to Philadelphia he was made professor of chemistry in the College of Philadelphia, and at the same time he opened an office for the practice of medicine. He married in 1776.

Rush was by nature a pious man, and he joined the Presbyterian church, stirred by the sermons of George Whitfield who preached in Philadelphia while Rush was a medical student. He was a reformer by nature, intolerant of the opinions of others, and with his views on alcohol and his disposition he would have doubtless been a leader in the Anti-Saloon League had he lived today. He was deeply interested in politics

and was a great talker; he was also an editor, an educator and an author, but first of all he was a hard-working, conscientious physician. John Adams wrote of him, "He is an elegant, ingenious body, a sprightly pretty fellow. He is a Republican. . . . But Rush I think is too much of a talker to be a deep thinker; elegant not great."

His political and official life was full of activity and change. In 1775, he was surgeon of a fleet of gunboats, then a member of a committee in charge of the manufacture of salt peter, then a member of the Provincial Congress, in which capacity he moved the appointment of a committee to draw a declaration on the question of independence, of which he was later a signer. He served in the army, and in 1777 was surgeon-general of the armies of the Middle Department; then he was physician-general to the military hospitals in the same district. He resigned from this position in 1778, after having accused Shippen of malpractice in the matter of hospital supplies. Shippen was acquitted. He wrote an unsigned letter to Patrick Henry full of criticism of the way the troops were handled. This was sent to Washington, who recognized the handwriting, and Rush, in disfavor, returned to practice and teaching, but he was back in the Pennsylvania General Assembly as delegate when the Federal Constitution was submitted for ratification. Later his political services were rewarded in his appointment as treasurer of the United States mint, which he held for fourteen years.

Rush was prominent in medical education, and the following paragraph from "Pediatrics of the Past" is as short a statement as can be made:

> When the Assembly dissolved the Board of Trustees and the Faculty in 1779 he was out of a teaching position. The University of Pennsylvania was formed and Rush was not given a position on account of the offense he had given in his letter when he first declined to serve in the new institution. In 1789, the College of Philadelphia was given back its charter, building and funds, and Rush resumed his old position, subsequently was made professor of the theory and practice of medicine and when in 1791 the College and the University were united, the title of his chair was changed to professor of the institutes of medicine and clinical practice; later he was made professor of physic to fill the place left vacant by the death of Adam Kuhn. Rush remained in these positions until he died. Rush was physician in the Pennsylvania Hospital and was largely instrumental in founding the first dispensary in this country, the Philadelphia dispensary.

Rush has been called the American Sydenham as he was a keen observer, but his therapeutics were of the Sangrado type. Like Lettsom he used vomits, purges and sweats and other strenuous measures. He wrote much and, contrary to the rule of the day, entertainingly; his books cover a wide range of subjects, from education to summer diarrhea, and include books or papers on many diseases; in addition, alcohol, slavery, war and the death penalty were favorite topics. His work on

insanity was for a long time a much used book. He wrote on yellow fever, and his "An Account of the Bilious Remitting Yellow Fever as It Appeared in the City of Philadelphia in the Year 1793" brought him a diamond from the Czar of Russia and medals from Prussia and Etruria. Later two medals in his honor were issued by the mint. Rush also called attention to the relation of diseased teeth to arthritis and its cure by their removal.

His most important pediatric work was his account of summer diarrhea, and he was the first to connect it with hot weather. Diarrhea is mentioned by most of the early writers on pediatrics, but little attention was paid to its cure or prevention.

AN INQUIRY

INTO

THE CAUSE AND CURE

OF

THE CHOLERA INFANTUM.

BY this name I mean to designate a disease, called, in Philadelphia, the "vomiting and purging of children." From the regularity of its appearance in the summer months, it is likewise known by the name of "the disease of the season." It prevails in most of the large towns of the United States. It is distinguished in Charleston, in South Carolina, by the name of "the April and May disease," from making its first appearance in those two months. It seldom appears in Philadelphia till the middle of June, or the beginning of July, and generally continues till near the middle

His paper, of which extracts follow, was entitled:

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By this name I mean to designate a disease, called in Philadelphia, the "vomiting and purging of children." From the regularity of its appearance in the summer months, it is likewise known by the name of "the disease of the season." It prevails in most of the large towns of the United States. It is distinguished in Charleston, in South Carolina, by the name of "the April and May disease," from making its first appearance in those two months. It seldom appears in Philadelphia till the middle of June, or the beginning of July, and generally continues till near the middle of September. Its frequency and danger are always in proportion to the heat of the weather. It affects children from the first or second week after their birth, till they are two years old. It sometimes begins with a diarrhœa, which continues for several days without any other symptom of indisposition; but it more frequently comes on with a violent vomiting and purging, and a high fever. The matter discharged from the stomach and bowels is generally yellow or green, but the stools are sometimes slimy and bloody, without any tincture of bile. In some instances they are nearly as limpid as water. Worms are frequently discharged in each kind of the stools that has been described. The children in this stage of the disease, appear to suffer a good deal of pain. They draw up their feet, and are never easy in one posture. The pulse is quick and weak. The head is unusually warm, while the extremities retain their natural heat, or incline to be cold. The fever is of the remitting kind, and discovers evident exacerbations, especially in the evenings. The disease affects the head so much, as in some instances to produce symptoms not only of delirium, but of mania, insomuch that the children throw their heads backwards and forwards, and sometimes make attempts to scratch, and to bite their parents, nurses, and even themselves. A swelling frequently occurs in the abdomen, and in the face and limbs. An intense thirst attends every stage of the disease. The eyes appear languid and hollow, and the children generally sleep with them half closed. Such is the insensibility of the system in some instances in this disease, that flies have been seen to alight upon the eyes when open, without exciting a motion in the eyelids to remove them. Sometimes the vomiting continues without the purging, but more generally the purging continues without the vomiting, through the whole course of the disease. The stools are frequently large, and extremely fetid, but in some instances they are without smell, and resemble drinks and aliments which have been taken into the body. The disease is sometimes fatal in a few days. I once saw it carry off a child in four and twenty hours. Its duration is varied by the season of the year, and by the changes in the temperature of the weather. A cool day frequently abates its violence, and disposes it to a favourable termination. It often continues, with occasional variations in its appearance, for six weeks or two months. Where the disease has been of long continuance, the approach of death is gradual, and attended by a number of distressing symptoms. An emaciation of the body to such a degree, that the bones come through the skin, livid spots, a singultus, convulsions, a strongly marked

hippocratic countenance, and a sore mouth, generally precede the fatal termination of this disease. Few children ever recover, after the last symptoms which have been mentioned make their appearance.

* * * * * *

I shall conclude this inquiry, by recommending the following methods of preventing this disease, all of which have been found, by experience to be useful.

1. The daily use of the cold bath.

2. A faithful and attentive accommodation of the dresses of children to the state and changes of the air.

3. A moderate quantity of salted meat taken occasionally in those months in which the disease usually prevails. It is perhaps in part from the daily use of salted meat in diet, that the children of country people escape this disease.

4. The use of sound old wine in the summer months. From a teaspoon full to a half a wine glass full, according to the age of the child, may be given every day. It is remarkable, that the children of persons in easy circumstances, who sip occasionally with their parents the remains of a glass of wine after dinner, are much less subject to this disease, than the children of poor people, who are without the benefit of that article of diet.

5. Cleanliness, both with respect to the skin and clothing of children. Perhaps the neglect of this direction may be another reason why the children of the poor are most subject to this disease.

6. The removal of children into the country before the approach of warm weather. This advice is peculiarly necessary during the whole period of dentition. I have never known but one instance of a child being affected by this disease, who had been carried into the country in order to avoid it.

I have only to add to the above observations, that since the prevalence of the yellow fever in Philadelphia after the year 1793, the cholera infantum has assumed symptoms of such malignity, as to require bleeding to cure it. In some cases, two and three bleedings were necessary for that purpose.

News and Comment

GENERAL

Second International Congress of Pediatrics.—The Department of State of the United States has named the following as delegates to the Second International Congress of Pediatrics, at Stockholm, August 18 to 21: John Foote, M.D., Washington, D. C.; Surgeon Grover A. Kempf, United States Public Health Service, and Clifford G. Grulee, M.D., Chicago.

Dr. Blanco Named Head of Children's Service in Buenos Aires Hospital.—Dr. Leon Velasco Blanco has been appointed head of the children's service of l'Hospital Torcuato de Alvear, Buenos Aires. His appointment was celebrated by his colleagues and friends with a banquet.

Board of Examiners Appointed.—The National Board of Medical Examiners has just announced new appointments. It is noteworthy that the only member of the Board of Examiners who can be regarded as a pediatrician is Dr. J. Gurney Taylor, who has received an appointment as a member of the Wisconsin State Board of Medical Examiners. It is a peculiar fact that the National Board of Medical Examiners is so little interested in children and the White House so much.

Inter-State Postgraduate Medical Association.—The International Assembly of the Inter-State Postgraduate Medical Association of North America meets in Minneapolis from October 20 to 24, 1930. Among the pediatricians who will address the meeting are: Dr. Isaac A. Abt, Chicago; Dr. Alan Brown, Toronto, and Dr. Fritz B. Talbot, Boston.

UNIVERSITY NEWS

The University of California announces the following appointments: Dr. Esther Rosencrantz, associate professor of medicine; Dr. Francis S. Smyth, associate professor of pediatrics; Dr. Alfred H. Washburn, associate professor of pediatrics; Dr. Merry Meryl Morris, assistant clinical professor of pediatrics; Dr. Lloyd E. Hardgrave, assistant clinical professor of pediatrics, and Dr. Kunisada Kiyasu, assistant clinical professor of pediatrics.

Ann S. Minot, Ph.D., has been appointed assistant professor of pediatric research at Vanderbilt University School of Medicine.

Abstracts from Current Literature

Pathology, Bacteriology and Biochemistry

THE EFFECT OF RACHITIC DIETS ON EXPERIMENTAL TUBERCULOSIS: III. RESISTANCE TO TUBERCULOSIS DECREASED BY ADDING CODLIVER OIL. IV. EFFECTS OF DISTURBING OPTIMAL RATIO BETWEEN CALCIUM, VITAMIN C AND VITAMIN D. AGNES G. GRANT, Am. Rev. Tuberc. **21**:102, 115 (Jan.) 1930.

A long series of studies with white rats showed that their resistance to tuberculosis can be largely dependent on the maintenance of an adequate ratio between the calcium, vitamin C and vitamin D of the diet. Rats are very resistant to tuberculosis, and in the first report of this series it was shown that they can be made immune to large subcutaneous doses of tubercle bacilli by giving an adequate diet both before and after inoculation. Deficiencies of both calcium and vitamin D in the diet make white rats so susceptible to tuberculosis that they develop lesions in the lungs when given comparatively small subcutaneous doses of tubercle bacilli. Further studies showed that a prolonged deficiency of vitamin D alone favors the development of a chronic type of tuberculosis in the lungs. In these two studies the lungs of infected rats were partially consolidated, with small areas that were tuberculous, even on gross examination. In the third report it was shown that, after rats have been made susceptible to tuberculosis by prolonged deficiency of vitamin D in the diet, their natural immunity is not restored by the addition of cod liver oil to the diet. They are made very resistant to rickets, but their susceptibility to tuberculosis is increased. This confirmed a previous observation that a prolonged excess of vitamin D in the diet of the mother, or the addition of this vitamin after a prolonged deficiency, decreased the resistance of young rats to tuberculosis. The addition of cod liver oil to diets that had been deficient in this factor changed the type of infection in the lungs. Instead of being partially consolidated, with areas that were grossly tuberculous, these lungs were large and well developed, with no areas of congestion or consolidation. In some the only visible lesions were a few dark miliary spots scattered over the posterior surface, and in some there were no gross lesions of any kind. Yet some of these lungs were filled with extensive and deep-seated lesions of tuberculosis that were very suggestive of the tuberculosis in the human host when examined microscopically. The addition of vitamin D to the diet, after prolonged deficiency of this factor, accentuates the need of white rats for vitamin C and makes them susceptible to deficiency. This combination of abundance and deficiency increases the susceptibility to tuberculosis. Work with tuberculosis in guinea-pigs shows that an excess of vitamin D is harmful whenever there is even comparative deficiency of vitamin C. Vitamin C influences the course of tuberculosis to such an extent that the disease cannot be successfully treated unless there is an abundance of this factor in the diet. In the fourth study it was shown that resistance to tuberculosis in white rats can be decreased from a natural immunity to moderate susceptibility, without destroying the growth impulse, by a prolonged disturbance in the optimal balance between the calcium, vitamin C and vitamin D in the diet. A prolonged excess of vitamin D in the diet, either with a deficiency or a normal amount of calcium hastens the spread of tuberculosis through the lungs. The substitution of vitamin C for vitamin D at the time of inoculation or the addition of vitamin C to a diet deficient in vitamin D tends to increase rather than decrease the amount of tuberculosis in the lungs. The addition of vitamin C to a diet containing vitamin D tends to correct the diet, and to increase the resistance to tuberculosis.

SMITH, Ogden, Utah.

THE EFFECT OF ULTRAVIOLET LIGHT ON CORNEAL TUBERCULOSIS IN RABBITS. H. F. NEWTON, Arch. Surg. **18**:1542, 1929.

When tubercle bacilli are injected into the cornea and then exposed to ultraviolet irradiations, before the cornea show a gross tuberculous lesion, the bacilli are destroyed and corneal tuberculosis is prevented. On the other hand, if the lesion has developed, ultraviolet irradiation does not sterilize the cornea and even accelerates the ulceration and exudate.

ENZER, Milwaukee.

THE SPECIFICITY OF SCARLATINAL HEMOLYTIC STREPTOCOCCI. GEORGE MORIWAKI, J. Bact. **18**:139, 1929.

In no respect has an absolute specificity of scarlatinal hemolytic streptococci been established. Every biologic as well as antigenic property tested seems common to a certain extent among strains of hemolytic streptococci from various sources. Especially, it is worth while to note that the rash-developing property is not limited to scarlatinal strains. These facts superficially seem to show that hemolytic streptococci primarily have no relation to the etiology of scarlatina, as was believed by Jochmann and others. But on the other hand, the fact that filtrates of broth culture of scarlatinal hemolytic streptococci contain scarlatinal antigen is well established, as shown by their rash-developing property and Schultz-Charlton's blanching phenomenon. Hemolytic streptococci from other sources also produce such an antigen. Therefore, the presence of a special filtrable virus of scarlatina may be doubted simply because the presence of such special virus, if any, together with streptococci from other sources than scarlatina is difficult to understand. The rash-developing power and the property of evoking Schultz-Charlton's phenomenon are properties of scarlatinal hemolytic streptococci, but these properties are common to hemolytic streptococci from other sources though in quantitatively less degree. Is there an unknown virus which makes hemolytic streptococci active? This is another problem. Finally the question arises as to the nature of scarlatinal symptoms. Are they toxic or allergic in relation to the product of the scarlatinal strain? The question has to be decided by further experimental studies.

AUTHOR'S SUMMARY.

BACTERIOLOGY OF THE BLOOD AND JOINTS IN RHEUMATIC FEVER. RUSSELL L. CECIL, EDITH E. NICHOLLS and WENDELL J. STAINSBY, J. Exper. Med. **50**:617, 1929.

During the spring of 1928, twenty-nine patients with acute rheumatic fever were subjected to blood cultures, of whom nine, or 31 per cent, yielded a streptococcus. During the spring of 1929, thirty-one patients with acute rheumatic fever were studied by blood cultures, of whom twenty-six, or 83.9 per cent, yielded a streptococcus. The higher percentage of positive cultures in the 1929 series appears to have been due to improved cultural methods. Of the thirty-five strains of streptococci recovered from blood cultures, thirty-three have been classified as alpha streptococci (*Streptococcus viridans*); one as a beta streptococcus (*Streptococcus hemolyticus*); and one a gamma streptococcus (*Streptococcus anhemolytius*). Some of the viridans strains produced very little green on blood mediums. Agglutination and absorption tests indicate that the strains of *Streptococcus viridans* recovered from the blood of patients with rheumatic fever show a tendency to fall into specific biologic groups. In seven patients with rheumatic fever who were subjected to cultures from affected joints, five, or 71.4 per cent, yielded *Streptococcus viridans*. In three patients in whom green streptococci were recovered from both the blood and joint, agglutination and absorption tests proved the identity of the strains isolated from the two sources. These observations corroborate those of previous investigators and make it difficult to escape the conclusion that rheumatic fever is a streptococcal infection, usually of the alpha or viridans type. The pathogenesis of rheumatic fever in respect to the joint

lesions appears to be analogous to that of infectious arthritis and gonococcal arthritis. Bacterial allergy probably influences the clinical picture in all three conditions, but in each instance the joint manifestations are primarily dependent on localization of bacteria in the joint, with subsequent infection.

AUTHORS' SUMMARY.

INTRADERMAL IMMUNIZATION OF MONKEYS WITH ONE SET OF INJECTIONS OF POLIOMYELITIS VIRUS. C. P. RHOADS, J. Exper. Med. **51**:1, 1930.

By means of a single large dose of poliomyelitis virus, distributed at a number of intradermal sites, active immunity has been produced in *Macacus rhesus* monkeys, as shown by skin neutralization and intracisternal tests. In the small series (four animals) of monkeys so treated, neither abortive nor paralytic signs of experimental poliomyelitis appeared.

AUTHORS' SUMMARY.

STUDIES ON INFLAMMATION: II. A MEASURE OF THE PERMEABILITY OF CAPILLARIES IN AN INFLAMED AREA. V. MENKIN and M. F. MENKIN, J. Exper. Med. **51**:285 (Feb.) 1930.

By a colorimetric method the rate of fall of concentration of trypan blue in capillaries was observed to be approximately twice as great in capillaries of inflamed tissue as in normal capillaries.

JAMIESON, Detroit.

THE BACTERIAL GROWTH INHIBITOR (LACTENIN) OF MILK. F. S. JONES and HENRY S. SIMMS, J. Exper. Med. **51**:327, 1930.

In this paper, the substance in milk which inhibits bacterial growth is called lactenin. It is stable for one and a half hours at p_H 4 and at p_H 10 and for longer periods in neutral solution. It is not associated with salts and carbohydrates and may be separated from them by dialysis. Lactenin is removed by agents which precipitate the proteins of whey. Part of these proteins may be hydrolyzed by tryptic digestion, and the resulting split products, together with the salts and sugar, may then be removed by dialysis without appreciable loss of lacteninic activity. This dialysis may be performed in a concentrating dialyzer, under sterile conditions and at low temperature, thus reducing the solution to small volume. The material may then be completely desiccated and kept three months with practically no loss of activity. The residue, on treating this dried material with salt solution, is 200 times as active as the original milk, on a dry weight basis. The size of the hemolytic zones of the scarlet fever streptococcus grown on a medium containing lactenin is found to furnish a simple and reliable measure of lacteninic activity.

AUTHOR'S SUMMARY.

A NEW MENINGOCOCCUS-LIKE ORGANISM (NEISSERIA FLAVESCENS N. SP.) FROM EPIDEMIC MENINGITIS. S. E. BRANHAM, Pub. Health Rep. **45**:845 (April 18) 1930.

Apparently a new type of organism was isolated in fourteen cases. The name *Neisseria flavescens* is proposed. Since 30 per cent of the cases from the locality (Chicago) belong to this group, and it is not represented in any of the polyvalent serums manufactured, it deserves attention.

SANFORD, Chicago.

AN ANEMIA OF DOGS PRODUCED BY FEEDING ONIONS. W. H. SEBRELL, Pub. Health Rep. **45**:1175 (May 23) 1930.

Cooked or raw onions, when given in quantities of 15 Gm. or more per kilogram of body weight per day, produced severe anemia in dogs. In amounts of 5 and 10 Gm. per kilogram of body weight cooked onions produced only slight anemia.

SANFORD, Chicago.

A Malignant Thymoma with Metastasis to the Central Nervous System in a Child Three and a Half Years Old. F. Danisch and E. Nedelmann, Virchows Arch. f. path. Anat. **268**:492, 1928.

The author discusses a malignant lymphocytoma of the thymus with metastases to the central nervous system, cervical lymph nodes, heart and kidneys. An interesting aspect of the case is a marked pleocytosis of the spinal fluid due to the presence of numerous tumor cells.

Hosoi, New York.

Chondroblastoma Growing in the Veins. M. Kósa, Virchows Arch. f. path. Anat. **272**:166, 1929.

In a girl, 13 years of age, a large tumor of the right femur grew through the lumen of the veins into the heart, even into the sinus venosus. The pulmonary arteries filled with tumor down to the capillaries. There was no destructive growth and no metastases; the tumor could be separated easily from the vessel wall. The tumor thrombus measured 70 cm. in length from the femur to the heart. The structure was that of different forms of cartilage, mostly adult. In the veins, the tumor had lost its blood vessels. It was, so to speak, a tissue culture of cartilage rather than a tumor.

Plaut, New York.

The Nature of the Toxicity of Mannite-Fermenting Dysentery Bacilli. A. de Assis, Ztschr. f. Immunitätsforsch. u. exper. Therap. **58**:343, 1928.

The toxicity of a recently isolated Hiss Y type strain was tested by the intravenous injection of mice with four preparations: (1) old bouillon culture filtrate; (2) filtrate of culture autolyzed in distilled water; (3) killed dried bacilli obtained by centrifuging a distilled water suspension; (4) wash water toxin, the supernatant of a centrifuged suspension of the bacteria dried, redissolved and centrifuged to clear of all insoluble material. Preparations 1 and 2 were nontoxic; 3 and 4 were toxic. Prolonged immunization of horses with these antigens gave negative results for antitoxin production. The author concludes that the toxicity of Hiss Y dysentery bacilli is bound up with the protoplasm and is not due to a toxin.

Avery, Nashville, Tenn.

Nutrition

Citrated Versus Acid Milk in Infant Feeding. Lloyd Arnold, Arch. Pediat. **46**:637 (Oct.) 1929.

The literature is reviewed, and the climatic factor and the acid-base content of the diet and their relation to digestion are discussed. The healthy infant possesses a stable autonomic nervous apparatus and can maintain itself in a perfect stable of equilibrium so long as the body receives the proper caloric and accessory food requirements. Such an organism will automatically adjust its gastro-intestinal tract to its food. If the infant is not in a state of physiologic equilibrium the power of adaptation is wanting.

Wilson, Norfolk, Va.

Supplying the Breast-Fed Baby with Vitamin B. J. H. West, Arch. Pediat. **46**:646 (Oct.) 1929.

Nursing mothers were placed on a liberal diet rich in vitamin B content. When complementary feedings were given the babies, wheat germ sugar or dried brewer's yeast was added. Only mothers having difficulty in nursing their babies were chosen in the series of forty-eight.

The author suggests that a vitamin-rich diet be given the prospective mother and as soon as possible during the puerperium. Babies are less fretful, and the necessity for complementary feedings is lessened.

Wilson, Norfolk, Va.

STUDIES ON THE EFFECTS OF OVERDOSAGE OF VITAMIN D. R. F. LIGHT, G. MILLER and C. N. FREY, J. Biol. Chem. **84**:487, 1929.

The administration of an excessive amount of viosterol may result in a drainage of mineral constituents from the body, with a relatively greater elimination of phosphorus than of calcium. The daily ingestion of 100,000 minimal effective doses may be followed in the rat by anorexia, emaciation, greasy hair, labored breathing and eventual death. No ill effects appear to attend the administration to the rat of 10,000 times the daily curative dose.

LOCKE, Chicago.

ALKALAEMIA IN THE DIARRHOEA OF INFANTS. MONTAGUE MAIZELS and CATHERINE B. MCARTHUR, Quart. J. Med. **23**:171 (Jan.) 1930.

The author's studies are related to an attempt to explain the condition of alkalemia associated with an acid reaction of the urine. Reference is made to the work of Hartmann and Smyth (AM. J. DIS. CHILD. **32**:1 [July] 1926) who attributed the phenomenon to retention of base by the kidney, depending on lowered osmotic pressure of the blood, depleted of its salts. It is the opinion of the authors that this explanation is not altogether correct. They believe that the condition is due to deficient excretion of base consequent on actual renal damage.

BRADFORD, Rochester, N. Y.

CALCIUM AND PHOSPHORUS METABOLISM IN CHRONIC DIARRHEA WITH TETANY. G. C. LINDER and CHARLES F. HARRIS, Quart. J. Med. **23**:195 (Jan.) 1930.

The authors present clinical and biochemical data concerning three cases of tetany occurring in adults with fatty diarrhea. The immediate cause of the tetany was ascribed to a deficiency in calcium. The serum inorganic phosphorus was reduced to a very low level, and in two of the cases it was almost absent from the urine. The various theories as to the causation of tetany associated with fatty diarrheas are discussed. The authors are inclined to consider the condition due to deficiency of vitamin D. The physical effect of the fats in impeding absorption of calcium may play a minor part. Treatment by restriction of fat and by large doses of viosterol was effective.

BRADFORD, Rochester, N. Y.

INDIGESTION IN CHILDREN FROM ONE TO FOURTEEN YEARS OF AGE. TAILLENS, Bull. Soc. de pédiat. de Paris **27**:241 (May 21) 1929.

The younger the child, the less he complains regarding indigestion. Rarely are there any subjective symptoms before the age of 8 years. The signs of indigestion in young children must be searched for and are often unrecognized. Indigestion with gastric hyperacidity is often mistaken for tuberculosis, and one third of these patients are sent to the hospital with conditions diagnosed as pulmonary or glandular tuberculosis, because they show a loss of weight and appear sickly. First, the indigestion is gastric, and as the trouble continues for months and years other conditions, particularly intestinal indigestion, are superadded. Indigestion is easily cured in children because it is a functional disorder. Hyperchlorhydria is the most serious disturbance in these patients. Of 200 children with indigestion, 90 per cent showed hyperchlorhydria, 8 per cent showed hypochlorhydria and 2 per cent had a normal acidity.

BENJAMIN, Montreal, Canada.

STIMULATING ACTION OF VITAMIN C IN CERTAIN FORMS OF CHRONIC INDIGESTION AND MALNUTRITION IN INFANCY. P. ROHMER, Bull. Soc. de pédiat. de Paris **27**:279 (May 21) 1929.

The author used Bezssonoff's extract of fresh cabbage. It consisted of a yellow powder, which he added to the diets of certain infants. By its use he obtained:

(1) a cure in infants with scurvy; (2) improvement in three patients with chronic intestinal indigestion (celiac disease) as shown by the stools, the general condition, the weight curves and the appetite, and (3) improvement in five patients ranging from 5 to 14 months of age, with malnutrition following digestive disturbances or infections. The latter patients failed to show any consistent gain in weight for several weeks despite the intake of a normal quantity of food, which they tolerated well; when the cabbage extract was added to the diets, they showed a consistent improvement in weight, appetite and general condition, and this improvement continued when the extract was discontinued, after it had been administered for periods ranging from twenty-three to sixty-nine days. To explain these good results the possible presence of a latent avitaminosis or scurvy is mentioned, but there were no observations of petechiae or hematuria to support such a theory. Rohmer thinks that the explanation is more probably to be found in some physiologic action of vitamin C about which knowledge is as yet inadequate.

BENJAMIN, Montreal, Canada.

CLINICAL AND EXPERIMENTAL OBSERVATIONS CONCERNING DRY MILK FEVER. M. H. DORLENCOURT, Bull. Soc. de pédiat. de Paris **27**:421 (Oct.) 1929.

Certain infants fed on dried milk have an unexplainable fever: they do not seem very ill, have a normal appetite and continue to gain weight consistently, and any symptoms that may be present, such as fretfulness, seem secondary to the fever. In all of the cases observed the fever did not come on immediately after the infant was given the dried milk, and there was always a latent period of days or even months before the onset of fever. On the contrary, any infant who has once developed this fever while on a diet of dried milk and who is not given dried milk for a time will develop fever immediately when again put on a diet of dried milk. The same effect can be produced by the use of any dried milk; occasionally, there is a latent period of a few days without fever when a change is made from one dried milk to another. The fever is not due to staleness of the milk powder, since the author fed some dried milk that was sixteen years old and had a rancid tallowy odor to an infant aged 3 months without producing any fever or intestinal disturbance.

The simplest explanation that suggests itself is that there might be some toxic pyretogenic substance in dried milk that causes the fever. This is not supported experimentally, as the author administered various extracts (acqueous, chloroform, ethereal, alcoholic, acetone) of dried milk to guinea-pigs and dogs, enterally and parenterally, without producing an elevation of temperature in any of them. He thinks that the phenomenon is due to a form of sensitization to some substances contained in dried milk. He does not mean, of course, the classic anaphylaxis to milk, in which there are present, in addition to fever, various skin eruptions, vomiting, diarrhea, etc. The antigen that produces the allergic response in the form of fever is probably formed during the process of preparation of the dried milk and is different from that which causes true anaphylaxis to milk itself. Such a form of allergy would explain the latent period, the cessation of fever when the dried milk is withdrawn from the diet and the fact that the same powder produces fever in one infant and not in many others. Skin tests made on three infants during the febrile stage as well as about ten days after the cessation of fever gave negative results, except for a weakly positive reaction in one case. Attempts at desensitization were made on two infants, but these were not observed long enough to draw any conclusions.

BENJAMIN, Montreal, Canada.

EXCESSIVE DOSES OF VITAMIN D. M. PINCHERLE and V. NAVA, Riv. di clin. pediat. **28**:177 (March) 1930.

The authors review the literature on the dangers of excessive doses of vitamin D, and report observations that they have made with white mice.

To produce definite damage in the white mouse, relatively huge doses of viosterol were necessary. The lesions consisted of excessive deposits of calcium in the epiphyseal zone of the bones and perhaps to a slight degree in the vessels and organs. Histologically, the bones gave the appearance of irregularity at the epiphysis, changes that somewhat simulated those of rickets. There were histologic changes in the blood vessels, the kidneys and the spleen. The excessive doses of viosterol retarded growth, as shown by both weight and development; occasionally death occurred. Until further observations are made with non-irradiated ergosterol, the exact cause of the damage cannot be placed. There is an ample margin of safety between the antirachitic and the toxic doses of viosterol.

HIGGINS, Boston.

ACIDOSIS (ACETONEMIA) IN INFANCY: DOES IT OCCUR IN EPIDEMIC FORM? C. SAINZ DE LOS TERREROS, Arch. españ. de pediat. **13**:449 (Aug.) 1929.

Periods exist in which acetonemia appears with abnormal frequence in children. The author believes that extrinsic factors are responsible for its occurrence. It accompanies a prevalence of grip. The author puts forward the theory that a possible hepatopancreatic insufficiency is a result of this infection, which in turn leads to the development of the acidosis. He has treated patients with this condition successfully by the use of insulin, combined with alkaline therapy and a carbohydrate diet.

SCHLUTZ, Minneapolis.

FEEDING WITHOUT MILK IN INFANCY. R. M. LARRAIN, Universidad de Chile, Ciencias Med. (Nov.) 1929.

Fifteen cases are reported in which Epstein's milkless feeding (zwieback pudding) was used; 9 patients were under 1 year of age and the remainder under 2 years. The caloric requirement and food elements were checked closely and the food manipulated daily to answer these requirements. The usual treatment lasted a month. It was thought to be indicated in digestive disturbances, milk idiosyncrasies, eczema, spasmophilia, exudative diatheses and anemia.

SANFORD, Chicago.

STUDIES ON CARBOHYDRATE-POOR NUTRITION. PAUL GYÖRGY and HERMANN KELLER, Biochem. Ztschr. **206**:120, 1929.

Young rats (from 15 to 25 days of age) show practically the same rate of growth on a practically carbohydrate-free diet as do other rats on a similar synthetic diet containing carbohydrate. Both kinds of diet, however, are inferior to a normal mixed diet. The practically carbohydrate-free diet has no hypoglycemic effect on the young growing rats or even a tendency toward lowering the blood sugar. The fat and protein metabolism must therefore completely satisfy the body's requirement for carbohydrate. Protein-rich feeding leads to relative hypertrophy of the kidneys. There is a caution against the application of the results of these studies to the feeding of infants, as the age of the experimental rats did not correspond to that period of growth.

KUGELMASS, New York.

PHYSICAL CHEMISTRY OF BODY FAT: A CONTRIBUTION TO THE PROBLEM OF THE PHYSIOLOGY OF FATTENING. WALTER SPRANGER, Biochem. Ztschr. **208**:164, 1929.

The viscosity of Ringer's solution is not noticeably altered by the addition of sodium oleate, calcium oleate, lecithin, cholesterol or cholesterol esters in physiologic concentrations. In the absence of neutral fat no antagonism is observed between these substances. Albumin, lecithin and sodium oleate in a physiologic model act as oil/water emulsifying agents. An increased addition of cholesterol

or lecithin causes not a greater dispersion of the fat but a separation of the phases that manifests itself in a fall of viscosity. Cholesterol esters are even more strikingly effective in this respect than the cholesterol. By reducing the water-protein-lecithin phase and increasing the fat quantity, the cholesterol ester produces separation and actual reversal of phase from the oil/water to the water/oil. The optimum condition for the oil/water emulsion exists when only about 60 per cent of the total cholesterol is in the form of esters and the rest is free, and a shift in proportion in either direction leads to separation and reversal of phases. In the body fat depots, the emulsion behaves like a water in oil emulsion.

KUGELMASS, New York.

THE ARTIFICIAL FEEDING OF INFANTS. H. BEUMER, Deutsche med. Wchnschr. **56**:44 (Jan. 10) 1930.

The author reports good results with the use of lactic acid milk made according to the method of Marriott. He has used it for a period of six years in dispensary, hospital and private practice.

SCHERER, Duluth, Minn.

THE DIETETIC MANAGEMENT OF DIARRHEAL DISTURBANCES IN INFANCY WITH CASEIN-FREE INITIAL DIET. LEOPOLD MOLL, Jahrb. f. Kinderh. **122**:253 (Jan.) 1929.

As an initial diet in acute diarrheal disturbances, one may use L. Moll's almond milk in younger infants; in older children a concentrated flour diet may be administered in the form of cake or rice pudding. These foods do not contain the injurious ingredients of milk, produce a certain effect on the diarrhea, and prevent severe loss in weight as well as qualitative and quantitative undernourishment. The diet is maintained for fourteen days; then it may be replaced by the original diet.

A. F. ABT, Chicago.

LIVER THERAPY IN SCORBUTUS. H. ARON, H. HIRSCH-KAUFFMANN and E. SCHÄDRICH, Jahrb. f. Kinderh. **123**:1 (Feb.) 1929.

Aron, Hirsch-Kaufmann and Schädrich state that fresh calves' liver and a freshly prepared cold water extract showed marked antiscorbutic properties in experiments on guinea-pigs. After heating the preparation for five minutes in a water-bath, this property is not lost. The alcohol extract, the residue of this extract and the commercial hepatrat do not evince antiscorbutic properties. It is yet to be determined whether there is a pure vitamin C effect here or a combination of vitamin factors.

A. F. ABT, Chicago.

BASAL METABOLISM IN CHILDREN. ZOLTÁN VON BÓKAY, Jahrb. f. Kinderh. **123**:10 (Feb.) 1929.

According to von Bókay, studies of basal metabolism are also of diagnostic value in pedriatrics, although standard figures here are as yet undetermined. Only comparatively large deviations from normal (20 per cent) are of diagnostic significance. There are various difficulties and sources of error in the determination of the actual basal metabolic rate: direct oxygen and carbon dioxide estimation should be possible by the apparatus used, so that hyperventilation may be recognized. Muscular activity and regulation respirations should be watched for. There should be several preliminary attempts in order to accustom the patient to the apparatus.

A. F. ABT, Chicago.

HAS IRRADIATED ERGOSTEROL BEEN ADMINISTERED IN UNNECESSARILY LARGE DOSES? P. GYÖRGY, Klin. Wchnschr. **8**:684 (April 9) 1929.

The heretofore prescribed doses of irradiated ergosterol have been excessive. The maximal therapeutic dose need not exceed 1 mg. per day. Recovery from

rickets is perhaps slower than with the larger doses, but the therapy is certain and harmless. In very severe cases of rickets, with tetany, the patients should be given from 2 to 3 mg. daily for a short time. It appears as if from 0.1 to 0.5 mg. per day is an ample prophylactic dose. The administration of from 2 to 4 mg. per day does not elevate the calcium content of the serum and does not produce deleterious effects. Injury from this treatment has been due entirely to excessive dosage.

KUGELMASS, New York.

EXPERIMENTAL STUDIES ON IRRADIATED ERGOSTEROL. PROPHYLAXIS. H. EUFINGER, H. WIESBADER and L. FOUSSEAU, Klin. Wchnschr. **8**:826 (April 30) 1929.

Colostrum or milk obtained from healthy human mothers does not contain sufficient vitamin D to cure severe rickets in rats. It is possible to enrich these excretions with vitamin D by feeding irradiated ergosterol. The transfer appears to be an immediate one because rats with severe rickets can be completely cured by feeding with colostrum or milk from a human mother who has been taking irradiated ergosterol for only a few days.

KUGELMASS, New York.

THE EFFECT OF AN EXTRACT OF THE ANTERIOR LOBE OF THE HYPOPHYSIS ON THE EXCRETION OF MILK. F. GRÜTER and P. STRICKER, Klin. Wchnschr. **8**:2322, 1929.

A hormone of the anterior lobe of the hypophysis has a stimulating effect on the mammary glands. Probably at the time of birth it stimulates the secretion of milk. Extracts from the liver, the lungs, the posterior lobe of the hypophysis and even the placenta are without such effects.

AUTHORS' SUMMARY.

DIAGNOSTIC AND CLINICAL SIGNS OF CONGENITAL DUODENAL STENOSIS. G. WEBER, Monatschr. f. Kinderh. **45**:208 (Nov.) 1929.

The reports of three cases of congenital duodenal stenosis are given, with case histories, roentgenograms and diagrams.

The author also reviews the literature. The stenosis can result from actual atresia of the duodenum or can be produced by constriction from sources external to the intestine. Vomiting is an important symptom but is not absolutely necessary at the beginning. Of course the greater the constriction the earlier the vomiting. The vomiting is not as explosive as in pylorospasm.

Diagnosis is most satisfactory by the use of roentgenograms. The prognosis depends on the degree of the occlusion, and the condition of the child when an operation is employed. Gastro-enterostomy seems to be the operation of choice.

GERSTLEY, Chicago

THE RÔLE OF THE HEMATO-ENCEPHALITIC BARRIER IN THE NEUROTOXIC SYNDROME OF ACUTE NUTRITIONAL DISTURBANCE. S. J. SCHAFERSTEIN, Monatschr. f. Kinderh. **45**:422 (Dec.) 1929.

The nervous symptoms in alimentary intoxication have been ascribed to a number of influences. The most popular explanations are anhydremia, colloid changes in the brain and also a lowering of the barrier between the blood and the brain tissues. The latter would permit toxins to pass through into the cerebrospinal fluid. Such a change has been described in many conditions, both infectious and metabolic.

Bessau in collaboration with Rosenbaum has shown in experiments on dogs that dehydration increases the permeability of the barrier and that a combination of desiccation and toxins of *Bacillus coli* produces a typical alimentary intoxication.

To determine whether there is a change in this barrier in the intoxication of infants, the writer injected uranium intramuscularly, followed in forty minutes by a lumbar puncture. It was necessary first to determine the minimal dosage of uranium. The former dose of 0.03 per kilogram was found to be too large and was reduced to 0.02 per kilogram. Further experiments reduced this to 0.015 as a minimum. In a number of cases a dosage of 0.02 was positive, while 0.015 gave negative results.

Having established the normal condition, Schaferstein tested patients with intoxication, dyspepsia, colitis and pneumonia. In practically all cases with toxic symptoms, a dosage of 0.015 gave positive results in the spinal fluid, proving a lowering of the barrier. Indeed this change was noticed when toxic symptoms developed in a nontoxic case.

There was no relation between the increase of permeability and the intensity of the toxic symptoms. In most of these cases there was an increase in the pressure of the spinal fluid.

The fact that the permeability of the barrier is affected by so many influences lowers its diagnostic value in meningitis.

GERSTLEY, Chicago.

A COMPARISON OF THE EFFECTS OF NÄHRZUCKER AND BEET SUGAR. S. J. SCHAFERSTEIN, Monatschr. f. Kinderh. **46**:385 (March) 1930.

The writer first reviews the literature concerning the effect of various sugars on the intestinal tract of the infant. As the intestinal digestion of various carbohydrates does not vary as greatly as was previously considered, he contrasted the speed of their absorption.

To 100 cc. of water he added 10 Gm. of the sugar to be tested and than made blood sugar determinations in fifteen, thirty, sixty and ninety minutes. His curves include those for Nährzucker, beet sugar and rice gruels.

In other experiments he added the sugars to albumin milk, breast milk and buttermilk. He conducted these experiments on normal children as well as on children with various types of nutritional disturbance.

In sixty-eight such determinations the writer concluded that the glycemic curve of ordinary beet sugar, in all the formulas in which it was administered, was practically identical with that of Nährzucker.

GERSTLEY, Chicago.

THE ANTIKETOGENIC EFFECT OF LACTOSE AND GALACTOSE IN NURSLINGS. GEORG BISCHOFF and KARL HIESTERMANN, Monatschr. f. Kinderh. **46**:426 (March) 1930.

So much objection has been raised to the use of milk sugar in artificial feeding that it has been almost completely discarded. One of the objections raised is that neither lactose nor galactose exert an antiketogenic effect.

By a restriction of diet, the writers produced an acetonuria in normal babies. Then the sugar to be tested was added in doses of 3, 5, 8 and 10 Gm. It was found that lactose and galactose were equally as efficient as dextrose in their antiketogenic effect.

Incidentally, the writers note that the organism has less tolerance to galactose than to the other sugars. In general, the border is about 0.3 Gm. per kilogram per hour.

GERSTLEY, Chicago.

RAW FOOD IN INFANT FEEDING. M. E. BIRCHER, München. med. Wchnschr. **77**: 19 (Jan. 3) 1930.

Bircher fed forty-six infants, between 1 and 6 months of age, on a diet of almond milk (in the absence of breast milk), fruit and vegetable juices. Some were given exposure to ultra-violet rays. The development was normal, and the incidence of infection low.

BRAHDY, Mount Vernon, N. Y.

CLINICAL AND EXPERIMENTAL RESEARCHES ON THE COURSE OF THE ALIMENTARY BLOOD SUGAR CURVE IN CHILDREN, ESPECIALLY IN THOSE WITH INCREASING OBESITY. GEORGE ERB, Ztschr. f. Kinderh. **48**:291, 1929.

The fasting values of blood sugar may vary in one and the same person in a very short time. To judge the condition of obese children, the consideration of the whole course of the alimentary blood sugar is important. In obese children who are treated successfully, there is at first a slow rounding off of the alimentary hyperglycemia, and later a secondary wave. In a case of pathologico-anatomic obesity combined with ordinary obesity, in which the patient was treated for a long time, there was this kind of a curve. For an accurate insight of the treatment of obese children it is necessary to test the state of the alimentary blood sugar curve in definite periods of time during and after the treatment. The fasting value of blood sugar is increased in children in the stage of increasing obesity.

EMERSON, Boston.

Prenatal Conditions

DIAPHYSIAL ACLASIS: HEREDITARY DEFORMING ACHONDRODYSPLASIA. HARTZELL HARRISON RAY, Arch. Pediat. **47**:152 (March) 1930.

A case of diaphysial aclasis is presented, together with a survey of the literature. The etiology and the varied clinical manifestations of this condition are discussed.

A summary of fifty-seven cases reported in the American literature since 1917, arranged as to sex, heredity, age at onset and race, is made available by this article.

WADDELL, University, Va.

THE RELATION OF MATERNAL PELVIC DISEASE TO DEFORMITIES IN THE NEW-BORN. L. GOLDSTEIN and D. P. MURPHY, Surg. Gynec. Obst. **49**:804, 1929.

Three of 310 children born of women suffering from idiopathic uterine hemorrhage, myoma, adnexitis, amenorrhea or cancinoma of the cervix or vulva were deformed. The abnormalities included anencephaly, microcephaly and hydrocephaly. This incidence of gross deformities corresponds to the birth rate of malformed children in the general population, indicating that the presence of uterine or adnexal pathologic process has no relation to the production of deformities in new-born children.

LIEVENDAHL, Chicago.

AN UNUSUAL CARDIAC MALFORMATION: COR TRILOCULARE BIVENTRICULARE WITH MIRROR PICTURE DEXTROCARDIA. JEAN SMITH, Brit. J. Child. Dis. **27**:20 (Jan.-March) 1930.

A male infant with marked cyanosis died at the age of 52 hours.

At autopsy the heart showed only one auricle into which all the veins opened. The aorta arose from the right ventricle and the pulmonary artery from the left. A patent ductus arteriosus was found. The heart was not enlarged.

The left lung was considerably larger than the right, and the lobes of the liver were transposed. A cluster of ten splenuli was another abnormal observation.

LANGMANN, New York.

CONGENITAL ANOMALIES OF THE RIGHT COLON. THÉVENARD, Bull. et mém. Soc. de chir. de Paris **22**:107 (Feb. 21) 1930.

In a patient, aged 18 years, who presented symptoms of chronic appendicitis, the ascending colon was found looped. The outer (ascending) arm of the loop was fixed to the posterolateral wall and formed an angle of about 120 degrees

with the cecum; the inner arm was freely movable and lay anterior to the outer arm. A roentgenogram showed the same condition in a brother, aged 8 years.

BIEKER, St. Petersburg, Fla.

CASE STUDY OF MICROGNATHIA. E. ROVIRALTA, Bol. de la Soc. Catalana de pediat. **1**:19 (Jan.) 1928.

In order to diagnose this case the author first ruled out the infectious causes, such as otitis media and myositis, the traumatic causes, such as dislocation, fractures and contraction of scar tissue, and the neurologic causes. He came to the conclusion that the cause must be a traumatic arthritis involving the glenoid cavity and the head of the mandible. Treatment consisted of forced opening under anesthesia.

WATSON, Chicago.

MALDEVELOPMENTS OF THE LUNG. F. ALTMANN, Beitr. z. path. Anat. u. z. allg. Path. **82**:199, 1929.

On the basis of thirteen examples, most of them in new-born infants or still-born fetuses, Altmann makes a classification of maldevelopments of the lung into which he thinks most, if not all, of the previously described examples can be fitted. The maldevelopments are divided into two main groups: those characterized by disturbances of growth, and those characterized by failure of development of the epithelial or mesenchymal element in a circumscribed area with overgrowth of the other element. Cyst formation may occur in either group. The first group is subdivided into two groups. In one there is simple overgrowth of the bronchi and their end branches. This process may involve a restricted area or a whole lobe or lung. The bronchial overgrowth may be associated with varying degrees of incomplete differentiation. In the second subgroup there is localized overgrowth of the bronchial branches, with a failure of development of the terminal outgrowths of the bronchi. In the second main group the process is one of hyperplastic or blastomatous overgrowth in a localized area of elements normally present, but because of the proliferation of one or the other element the relationship of the tissue elements to each other is an abnormal one. The second main group is subdivided into two subgroups, depending on whether the epithelial or mesenchymal elements are hyperplastic. Two examples of mediastinal cyst are included; these the author is also able to place in his classification.

SCHULTZ, Chicago.

APLASIA OF THE THYROID IN RELATION TO ENDOCRINE FUNCTION DURING FETAL LIFE. E. J. KRAUS, Beitr. z. path. Anat. u. z. allg. Path. **82**:291, 1929.

In his discussion of the question whether the endocrine organs manifest their specific functions during fetal life, Kraus quotes the opinion of E. J. Thomas that these organs exhibit no activity during the fetal period under normal conditions, but that the fetus is dependent for its endocrine hormones on those of the maternal circulation. As a contribution to this question, he presents a study of a male infant 47 cm. long, who died on the day of birth. In addition to multiple anatomic maldevelopments, the following changes were noted in the endocrine system: complete aplasia of the thyroid, hypoplasia of the thymus, hyperplasia of the hypophysis and suprarenals. The parathyroids, the interstitial cells of the testes, and the islands of Langerhans were normal. The hypoplastic thymus revealed microscopic evidence of involution. The hyperplasia of the hypophysis involved the anterior lobe and was due to an increase in the number of large chromophobe cells. Both the cortex and medulla of the suprarenals were hyperplastic and the medulla gave the chrome reaction, which is accepted as evidence of epinephrine formation. Kraus interprets the changes noted in the

endocrine system as proof that a mutual inter-relationship of the organs of this system exists during fetal life and that the endocrine system functions specifically before birth.

SCHULTZ, Chicago.

UNIVERSAL CONGENITAL HYDROPS. H. HARTMANN, Zentralbl. f. Gynäk. **52**:299, 1928.

Hydrops congenitus is characterized by anasarca, hydrops of all cavities and myeloid foci in liver, spleen, kidney, suprarenal gland and intestine. The etiology is unknown. Syphilis is not the cause, but may produce similar changes. The frequent coincidence of congenital hydrops with maternal nephritis points to the existence of an etiologic connection between these conditions. A toxemia for which the fetus is probably responsible is regarded as the primary cause.

HUEBER, Chicago.

Diseases of the New-Born

IDIOPATHIC ANEMIA OF THE NEW-BORN INFANT. WILLIAM MORRIS HAPP, Arch. Pediat. **47**:171 (March) 1930.

A severe case of unexplained anemia in a new born infant is presented, together with summaries of the seven other cases reported in the literature. The author points out that many more similar cases would be noted were it customary to examine the blood of new-born infants. Transfusion of blood is recommended as the treatment of choice. It proved helpful in the case presented.

WARFIELD, University, Va.

CHILD LIFE INVESTIGATIONS: THE CAUSE OF NEO-NATAL DEATH. J. N. CRUICKSHANK, M. Res. Council, Report no. 145, 1930.

In 800 autopsies in cases of neonatal death, the cause of death was considered to be: (1) conditions due to birth asphyxia, birth injury or prematurity, 540 (67.5 per cent); (2) infective conditions, 238 (29.75 per cent), and (3) gross developmental defects, 22 (2.75 per cent).

In the first group 400 of the infants were premature. The number of deaths during the first week was 565 (70 per cent), during the second week 155 (19.4 per cent), during the third week 59 (7.3 per cent), and during the fourth week 21 (2.7 per cent). Of the aforementioned 540 infants, 244 (45.2 per cent) died on the first day, 57 (10.5 per cent) on the second day and 71 (13.1 per cent) on the third day. In the infective condition group, 64 infants (26.8 per cent) died during the first week, 99 (41.16 per cent) during the second week, 54 (22.6 per cent) during the third week and 21 (9 per cent) during the fourth week. Of deaths from developmental defects, 17 occurred during the first week, and 5 during the second. The presence of congenital syphilis was definitely established in less than 1 per cent of the cases in the whole series.

SANFORD, Chicago.

BIRTH OF HEALTHY QUADRUPLETS. THEODORE PSYCHARIOS, Bull. Soc. de pédiat. de Paris **27**:278 (May 21) 1929.

This was the mother's seventh pregnancy and she gave birth to four healthy boys. They weighed 2,350, 1,750, 2,400 and 1,800 Gm. in the order in which they were born. There was one elongated placenta which weighed 1,250 Gm., with four membranes. The mother, aged 35, born in Crete, had given birth to six normal children after six normal pregnancies, and she had had no miscarriages. Her mother had given birth to triplets, and a sister had been delivered of twins. The four boys thrived in a warm room (incubator) and were breast fed by the mother and two wet nurses.

BERGERIS, Montreal, Canada.

A New-Born Infant with Congenital Heart Disease. Buxo Izaguirre, Bol. de la Soc. Catalana de pediat. **1**:68 (Jan.) 1928.

A case of tetrology of Fallot is reported, in which convulsions started at the age of 6 days and produced death within twenty-four hours. The diagnosis was made by the history and the physical observations. Autopsy was not performed.

Watson, Chicago.

Histology of Cephalhematoma. O. Hatschek, Beitr. z. path. Anat. u. z. allg. Path. **82**:268, 1929.

Hatschek says that the histology of the reparative changes in cephalhematoma has not been previously described. He presents in detail a microscopic study of the process based on two examples. The first came from a child who lived seventeen days, the second from one who lived three months. In each case there was congenital internal hydrocephalus. In the first case there was an external and an internal hematoma; in the second case, only an internal one. In the first case, the bone between the central portions of the two hematomas was necrotic. Organization of the hematoma occurs at the periphery by the formation of cellular connective tissue. The pericranium or the dura, lifted off by the hemorrhage, acts as a cambium layer and forms new bone in the organization tissue. Toward the central portion, away from the lateral margins, the area of hemorrhage had become encapsulated by a thin layer of dense fibrous tissue. Connective tissue proliferation was no longer active in this tissue, but new bone formation was in process, both above and below the encapsulated hemorrhage. Red blood corpuscles had disappeared from the latter. The author believes that the hematoma must finally be replaced by new formed bone, which forms a layer considerably thicker than the normal skull. Although he has not seen the still later stages, he believes that the thick layer of new formed bone is gradually reduced to normal thickness by pressure exerted on its inner surface by the growing brain. He appends a description of the proliferative changes and new bone formation in a syphilitic cranial osteophyte into which hemorrhage had occurred at birth.

Schultz, Chicago.

Attacks of Apnea. A. Peiper, Jahrb. f. Kinderh. **123**:129 (March) 1929.

Peiper states that, according to experiments on animals by other authors, the respiratory center consists of several portions which embryologically are different and which may be separated according to function. Periodic respiration, such as Cheyne-Stokes' or Biot's type of breathing, is frequent in weak premature infants and is uninfluenced by the administration of lobeline and other measures. It should be considered as a relapse to a primitive form of breathing (pale encephalic reaction), in which the higher centers temporarily or permanently do not function and the lower centers govern the respiration. The attacks of asphyxia arise from the sudden cessation of function of all the divisions of the respiratory center. They occur most frequently in the first two weeks of life and occur most often in young infants in poor general condition and of subnormal in weight. The inciting cause may be the limitation of diaphragmatic motion in the ingestion of nourishment. After a period of asphyxia, there is a form of respiration with short, deep inspirations and minute-long pauses. With every inspiration the mouth is wide open, whereas ordinarily the mouth is closed.

Clinically and pathologically there is no evidence of cerebral hemorrhage as the cause of these attacks of apnea. These are only partial manifestations of the general lowering in the reflex irritability. The immature state of the infant's nervous system favors this course of events, since the particular centers are as yet loosely joined in functional activity and are readily separated from each other.

In the therapy, marked stimulation of the skin, such as hot and cold baths and spanking, are to be avoided. On the other hand, artificial respiration, administra-

tion of oxygen, 0.0039 Gm. of lobeline given intramuscularly, or 1 mg. of epinephrine injected intracardially are recommended. Because of the long pauses in respiration, it is sometimes difficult to decide exactly when death has occurred.

A. F. Abt, Chicago.

Grave Familial Icterus and Hydrops Congenitus Universalis Foetus. C. de Lange and A. K. W. Arntzenius, Jahrb. f. Kinderh. **124**:1 (May) 1929.

Microscopic examination of two cases of severe familial icterus showed a high grade blood destruction and blood regeneration. Lange and Arntzenius note that a gradual transition of icterus neonatorum to icterus familiaris gravior is improbable. Also in hydrops congenitus there is a definite blood destruction, as is demonstrated by the siderosis and pleochromic resorption icterus. Both diseases are of familial and hereditary origin and are induced by an intoxication of unknown nature. The history tends to point toward the mother as the source of the condition (abortions, macerated fetus, malformations).

A. F. Abt, Chicago.

Iso-Agglutination in the New-Born and Its Relationship to Icterus Neonatorum. G. Lenart and S. Biró, Jahrb. f. Kinderh. **124**:77 (May) 1929.

Lenart and Biró observe that an intensive icterus neonatorum occurred twice as frequently after agglutinophilic pregnancy. In five of fifty-six cases the maternal serum agglutinated the child's erythrocytes in spite of a homospecific pregnancy. In the child's serum there were two instances in which agglutinins were found which did not arise from the mother. In four cases free iso-agglutinins could be demonstrated in the serum infants in group I. To explain this the authors assume the existence of autochthonus fetal iso-agglutinins.

A. F. Abt, Chicago.

Cell Contents and Iron in the Spleen of Fetus and New-Born. I. E. Lewin, Virchows Arch. f. path. Anat. **273**:168, 1929.

In eighty-five fetuses and new-born infants the spleens were examined; thirty-five were mature and fifty were premature. The follicles are smaller in the new-born than in the adult; the external zone often is indistinct. Granulocytes are found in different numbers. Eosinophil cells are always present. Bosophils are few; they are found only after fixation in absolute alcohol. Their number does not increase with toxic conditions nor with congenital syphilis. Plasma cells are absent. No megakaryocytes are found. Immature red cells are found in varying numbers and varying distribution.

In the mature new-born the spleen generally gives a strong iron reaction. It was the same in the spleen of four infants born during the eighth and ninth month. In the spleen of forty-four immature infants and of four mature infants little or no iron was found (Hueck's iron reaction was used). In the sixth and seventh month the iron reaction is negative. Stasis and duration of labor bear no relation to the iron reaction. In two prematurely born infants there were hemorrhages in the spleen, but the iron reaction was negative. These results partly are at variance with those of Lubarsch.

Plaut, New York.

The Pathogenesis of Scleredema in Infants. Walter Heymann, Ztschr. f. Kinderh. **48**:238, 1929.

Scleremic tissue (cutis and subcutis) imbibes water in salt solution at different concentrations to a less extent than nonscleremic tissue. The degree of water intake in normal skin is dependent on the concentration of the salt surrounding it.

"The relative osmotic power of regulation" is hardly present in sclerema. These results are referred to a disturbance in the colloidal economy of the tissue water of the connective tissue of the skin, possibly in the sense that the ratio of imbibition water to solution water is displaced in favor of the imbibition water in sclerema.

EMERSON, Boston.

Acute Infections

FUNCTIONAL CIRCULATORY DISTURBANCES AND ORGANIC OBSTRUCTION OF THE CEREBRAL BLOOD VESSELS, WITH A CONTRIBUTION TO THE PATHOLOGY OF PERTUSSIS ECLAMPSIA. FRIEDRICH HILLER and ROY R. GRINKER, Arch. Neurol. & Psychiat. **23**:634 (April) 1930.

This article includes a full discussion of the problem of functional circulatory disturbances and their effect on the central nervous system. Various writers have pointed out that circulatory stasis and prestasis of the cortical vessels may result in organic changes in the brain as severe as organic circulatory disturbances, such as in thrombosis and embolism. The authors report a case of pertussis eclampsia in a girl, aged 3 years, and demonstrate the changes in the brain which they feel are explainable on the basis of stasis and prestasis of the cerebral blood vessels. For comparison they report a case of embolism with subsequent thrombosis and its changes in the brain. They point out the similarities and differences in the changes in the brain produced by the two conditions.

BEVERLY, Chicago.

EPIDEMIC CEREBROSPINAL FEVER ON THE PACIFIC COAST. J. C. GEIGER, California & West. Med. **32**:322 (May) 1930.

There has been a decided rise in the incidence of epidemic cerebrospinal fever for the Pacific Coast States beginning in 1926, and Oregon reported a rise in 1925. The increased incidence has been maintained for 1927 and 1928 for reported cases and deaths, and through the summer months of 1929. The two Pacific Coast ports most affected were Seattle and San Francisco. Among steerage passengers the disease was practically limited to those of one line, and was prevalent mainly among Filipinos arriving from Oriental ports. The measures advocated by health officials have apparently been successful, for all ships have arrived "clean" since sailing from Manila, as far back as May 11, 1929. The epidemic of this disease, which had been prevailing in Shanghai, passed its peak in April, and this may be significant in the light of the absence of recent cases on shipboard. The mortality for the cases on ship board was high. The mortality rate in California was 44 per cent in 1928, and 50.8 per cent during the epidemic period of 1929. The types isolated in the California outbreak of 1928 and 1929 were six strains of type one and five strains of type three, Gordon classification.

DICKEY, San Francisco.

THE PERIOD OF INFECTIVITY AND SERUM PREVENTION OF CHICKENPOX. JOHN E. GORDON and FRED M. MEADER, J. A. M. A. **93**:2013 (Dec. 28) 1929.

According to the authors, chickenpox is apparently infectious for not longer than twenty-four hours preceding the eruption. During convalescence, infectivity is less prolonged than is commonly supposed, but it does not necessarily coincide with the persistence of crusted lesions. The duration is probably ten days. The serum of convalescent patients confers immunity in a great majority of cases if obtained within a month of the appearance of the eruption. It is less efficient if obtained later, and after five months furnishes protection in only one third of the cases.

BONAR, Salt Lake City.

THE DICK TEST AND ALLERGIC SKIN REACTIONS TO STREPTOCOCCUS NUCLEOPROTEINS. K. ANDO, J. Immunol. **17**:361, 1929.

From the Dick toxin two substances have been obtained with which skin reactions can be produced in human beings: a nucleoprotein and a specific toxin. The so-called nucleoprotein causes a skin reaction that cannot be distinguished from that caused by ordinary Dick toxin; it is heat-stable and nontoxic for man; it does not cause any skin reaction in white pigs. By repeated alcohol and acid precipitation a relatively pure specific toxin can be obtained from culture filtrates of *Streptococcus scarlatinae;* this causes reactions in the skin of human beings and white pigs; it is destroyed by heating to 80 C. for thirty minutes, and its action is neutralized by scarlatinal antitoxin. Susceptible persons can be immunized with it. In the course of immunization the scarlatinoid syndrome was observed in some cases. No evidences of allergy could be obtained with the true toxin-exotoxin, but the nucleoprotein gave rise to an allergic condition, and a skin reaction to the protein may be regarded as allergic. The nucleoprotein may influence the reaction to the ordinary Dick toxin, especially if it is weak in true toxin. High dilutions of potent toxin should be used preferably, and the Washington standard toxin was found to be satisfactory as it contained traces only of nucleoprotein.

[ARCH. PATH.].

HYPERSENSITIVENESS TO DIPHTHERIA BACILLI. JAMES M. NEILL and WILLIAM L. FLEMING, J. Immunol. **17**:419, 1929.

The present example of diptheria bacterial hypersensitiveness agrees with the previous examples in that it is manifested by an immediate skin reaction and in that the capacity for the reaction can be passively transferred. It differs, however, in that the individual is particularly reactive with a heat-labile (60 C.) product not involved in the reactions of the previous diphtheria-sensitive persons. This product is apparently contained in effective concentration only in the indicated culture filtrates of toxicogenic diphtheria bacilli and not in the filtrates of nontoxicogenic strains nor in solutions of material derived from the washed bacterial cells. If it is not toxin, it is a hitherto unrecognized diphtheria bacterial product that possesses a degree of lability not usually encountered among the bacterial substances associated with hypersensitive reactions. The results are discussed in respect to the possibility that the described reactions may represent an example of true hypersensitiveness of man to diphtheria toxin.

AUTHORS' SUMMARY [ARCH. PATH.].

ON THE NATURAL IMMUNITY TO SCARLET FEVER OF THE JAPANESE AND CHINESE RESIDING IN SOUTH MANCHURIA. K. ANDO, H. NISHIMURA and K. OZAKI, J. Immunol. **17**:473, 1929.

According to the Dick skin test there is a considerable difference in the susceptibility to scarlet fever between the Japanese and the Chinese residing in South Manchuria. The difference in scarlet fever morbidity of these two cases may at least be partly explained by the difference in their susceptibility. No fact has been discovered which seems to indicate that there is a greater percentage of negative reactors among Japanese children who lived long or were born in Manchuria where scarlet fever is more prevalent than in Japan proper than among those who lived long in Japan proper and have immigrated only recently. It seems reasonable to suppose that the difference in susceptibility may indicate racial difference of "Antikörperbildungsbereitschaft" in the sense of Hirszfeld, but not dependent on the difference in "Umwelteinflüsse."

AUTHORS' SUMMARY [ARCH. PATH.].

OCCURRENCE AND MANIFESTATIONS OF THROMBOSES PARTICULARLY SINUS THROMBOSES, CEREBRAL AND DURAL HEMORRHAGES AND EMBOLISM AFTER THE ACUTE INFECTIOUS DISEASES. H. ZISCHINSKY, Jahrb. f. Kinderh. **124**: 35 (May) 1929.

Although in diphtheria, emboli from a cardiac thrombus are comparatively frequent, H. Zischinsky reports two cases in which there was toxic injury to the vessels, comparable to that occurring after pertussis. In 17,000 cases of scarlatina there were only four instances of venous thrombosis. Otogenous sinus thrombosis occurred only once, since in scarlatina there is relatively slight danger of mastoiditis.

Thromboses were observed in 2 of 2,400 cases of dysentery. Of 16 cases which occurred from one to six weeks after the onset of measles in children during the first four years of life, eight ran their course without cerebral symptoms.

Thromboses and hemorrhages occur most frequently after pertussis. The number of cough-spasms is not responsible for this, although subconjunctical hematomas frequently occur in children who cough slightly.

The real cause of these cerebral complications is a toxic injury of the vessels which results in subcutaneous hemorrhages, facial edema and "pertussis brain." Children in the first two years of life are most frequently affected. There were also extensive pulmonary changes in these children. The thromboses and meningeal hemorrhages usually occur from one to two months after the onset of the pertussis. Frequently there is cerebral edema. Usually there are general cerebral manifestations such as convulsions which may last twenty-four hours.

With sinus thrombosis there is simultaneously a toxic condition. In fifteen of the author's fifty-four cases the course was symptomless. Lumbar puncture was not of any great assistance. The occurrence of thromboses in other vascular regions speaks for a general vascular involvement in pertussis. The preponderance of cases of sinus thrombosis is due to the fact that in childhood there is a tendency to cerebral complications.

A. F. ABT, Chicago.

PERTUSSIS-ENCEPHALITIS IN CHILDHOOD. W. MIKULOWSKI, Jahrb. f. Kinderh. **124**:103 (May) 1929.

Mikulowski describes a case of encephalitis occurring six weeks after measles in a child, aged 2. Typical pertussis developed, and the condition was considered one of "pertussis brain."

A. F. ABT, Chicago.

THE PROPERTIES OF DIPHTHERIA TOXIN-ANTITOXIN MIXTURES. H. SCHMIDT and W. SCHOLZ, Ztschr. f. Immunitätsforsch. u. exper. Therap. **58**:98, 1928.

An otherwise fatal diphtheria toxin-antitoxin mixture appears under favorable experimental conditions as nontoxic for guinea-pigs, if the animals are sensitized with the normal serum homologous to the antitoxin. If the guinea-pigs are sensitized to another protein, then no difference is noticed between sensitized and untreated animals after the injection of the toxin-antitoxin. If the sensitized animals are desensitized through a reinjection of homologous serum, then they are relatively insusceptible to diphtheria toxin. The authors present the supposition that a resulting protein-antiprotein reaction takes place in the body and that certain toxin-susceptible cell groups important for the formation of antitoxin are blockaded. It is suggested that these facts be considered in the practice of active immunization against diphtheria.

AVERY, Nashville, Tenn.

THE COMPLEMENT-BINDING REACTION IN SCARLET FEVER. VON NAUMANN, Ztschr. f. Kinderh. **48**:157, 1929.

Complement-binding with specific streptococcic antigens has great practical diagnostic significance; it occurs after the first week and is reliable in the second

week; it is transient and usually disappears from the fourth week on. The reaction is distinguished from the Wassermann reaction in scarlet fever by its specific standardization. Syphilitic blood never gives a positive reaction with specific streptococcic antigens. Only occasionally, blood from a case of scarlet fever gives a positive Wassermann reaction as an expression of an unspecific overlapping of the complement-binding antibodies. The majority of streptococci isolated in cases of scarlet fever give reliable extracts, but occasionally they are given by other stpretococci which do not come from scarlet fever. The specific character of the reaction lies in the production of antibodies. In the other diseases, especially exanthemas caused by streptococci the author did not find any antibodies with a complement-binding reaction. Thus, the practical diagnostic value of the reactions is increased. By means of his method, it is possible to make a diagnosis in clinically doubtful cases of scarlet fever without a rash or with a questionable rash.

EMERSON, Boston.

PERCUTANEOUS IMMUNIZATION AGAINST DIPHTHERIA AFTER LÖWENSTEIN. H. BAAR AND A. GRABENHOFER, Ztschr. f. Kinderh. **48**:248, 1929.

By the percutaneous application of diphtheria toxoid, guinea-pigs are so immunized that they tolerate a multiple minimal necrotic dose without reaction, and also a multiple minimal lethal dose; they are resistant to an intraconjunctival infection with virulent diphtheria bacilli. From 50 to 60 per cent of the children immunized percutaneously give negative reactions to the Schick test within six weeks, and 75 per cent within four months. The degree of immunization increases with the number of treatments, and in children between the ages of 1 and 14 years it is independent of age. Among twenty cases of diptheria there was only one child who had had four treaments. Any noticeable amount of "silent immunization" could be excluded.

EMERSON, Boston.

A CASE OF DIPHTHERITIC BACTEREMIA DURING PARATYPHOID FEVER. M. FIDLER, Cas. lék. česk. **67**:369 (March 2) 1928.

In a medical student, a woman, the white blood cells increased from 4,100 to 6,700 during paratyphoid illness. The toxemia was out of proportion to the disease, and a tachycardia was explained on the basis of an enlarged thyroid. Grip was regarded as the association infection until diphtheritic organisms were found in the nasopharyngeal cultures. Klebs-Löffler organisms were recovered in the blood cultures. Because of sensitivity to horse serum, convulsions developed after slow intramuscular injection of only 3,500 units of antitoxin. Atropine and calcium had been given previously with a desensitizing dose of serum. Marked improvement with a recession of the typhoid resulted.

STEELE, Chicago.

Chronic Infections

TUBERCULOUS INFECTION IN INFANCY. J. A. MYERS and L. M. KERNAGHE, Am. Rev. Tuberc. **21**:423 (April) 1930.

The authors present a study of 532 infants, 236 of whom reacted positively to the tuberculin test. Clinical tuberculosis developed in a relatively small number of those traced after a period of years. The majority of this group infected in infancy are now apparently healthy. Many have never been ill, and are now of school age. Of the 172 who have been traced, only 6 have died of tuberculosis. The history of exposure was definite in 195 and questionable in 22 of the 236 reactors. Of the diagnostic procedures, the tuberculin skin test, roentgen examination and history of exposure were found to be of greatest value.

When infection has occurred, the first step in treatment is to prevent further exposure in so far as possible. Comfort of the infant, which means conservation of energy, proper diet for its age and heliotherapy when indicated are important.

SMITH, Ogden, Utah.

TUBERCULOUS INFECTION IN CHILDHOOD. J. A. MYERS, Am. Rev. Tuberc. **21**: 479 (April) 1930.

The author gives an analytic review of the literature, dealing especially with the incidence of tuberculin skin reactions in childhood and their interpretation and significance.

SMITH, Ogden, Utah.

TUBERCULOSIS AMONG GIRLS AND BOYS IN THEIR TEENS. J. A. MYERS and L. M. KERNKAMP, Am. Rev. Tuberc. **21**:509 (April) 1930.

In a study of 242 cases of tuberculosis in boys and girls from the teen ages to 21 years, the most significant early symptoms were pleurisy (36 per cent), hemorrhage (15 per cent) and fatigue. A history of exposure was obtainable in 59 per cent. Roentgenograms usually give more information than physical examinations, although neither can be absolutely relied on. Tuberculin test and laboratory examinations are of great value, and may occasionally furnish positive evidence when the clinical observations are apparently negative. Minimal tuberculosis is so elusive that every bit of evidence should be brought to light in suspected cases.

The significance of the childhood type of tuberculosis is indicated by the finding of evidence of this type in 76 per cent of this group, and lesions of both childhood and adult types in 60 per cent. Forty-two per cent showed the childhood type in one lung and the adult type in the opposite lung. It is obvious, therefore, that subjects with healed tuberculosis of the childhood type furnish at least 60 per cent of those who later develop the adult type of lesion.

Treatment should be instituted at the earliest possible moment when evidence of progressive tuberculosis is detected in boys and girls of the teen ages. The most drastic methods of treatment are none too drastic for this age group. Progress from the minimal to the far advanced stages is so rapid at this age that overconservatism is extremely dangerous. The authors believe that progressive tuberculosis occurring during the teen ages, and particularly among girls, even though the disease is minimal, is an indication for artificial pneumothorax.

SMITH, Ogden, Utah.

CHILDHOOD TUBERCULOSIS: ITS TREATMENT. CHARLES L. IANNE, California & West. Med. **32**:334 (May) 1930.

Rest and time are the chief factors to be stressed in the treatment for tuberculosis in childhood. These, with general hygienic measures, are common in the treatment for pulmonary disease in both children and adults, and in the lymphatic and bone manifestations of the disease. In addition to the measures mentioned, each type presents problems alien to the others. The place of the parents in the treatment is important, and the problem must be presented to them intelligently. The home and the school are the places where the principles of the treatment must be put into effect, and the preventorium should be resorted to only when rest and time fail.

DICKEY, San Francisco.

CHEST ROENTGENOGRAMS OF NONTUBERCULOUS CHILDREN SUSPECTED OF BEING TUBERCULOUS. ERNST WOLFF and ROBERT S. STONE, J. A. M. A. **94**:458 (Feb. 15) 1930.

There exists a marked confusion in the interpretation of the shadows in the roentgenograms of children's chests. Observations on ninety-three children sus-

pected of being tuberculous were compared with those made on twenty normal children. The roentgenograms of the chests of children without acute illness, with a negative tuberculin reaction may show single or multiple, large or small axial vessels in the hili, multiple axial vessels up to 2 or 3 mm. in diameter in the lung tissue, localized, increased lung markings, localized pleural thickenings or none of these shadows. It is therefore apparent that a diagnosis of tuberculosis of the mediastinal glands or lung tissue cannot be based on these observations. Calcification, glandular tumors or localized pulmonary infiltrations were not found. No definite correlation was found to exist between the positive roentgen observations and the clinical history.

BONAR, Salt Lake City.

A CLINICAL STUDY OF CONGENITAL NEURO-SYPHILIS: II, CONGENITAL TABES, TABO-PARESIS AND GENERAL PARALYSIS. FERGUS R. FERGUSON and MACDONALD CRITCHLEY, Brit. J. Child. Dis. **27**:1 (Jan.-March) 1930.

I. Eight cases of congenital tabes, a rare condition, were studied. The average age at onset was 17 years (extremes, 10 and 24 years). The first symptoms were failing vision and paresthesia. Severe lightning pains and ataxia were rare, later there were headache, photophobia and diplopia. Typical abnormalities were dilated pupils in four cases, strabismus in four and nystagmus in three. Optic atrophy was of frequent occurrence. There was absence or marked diminution of the tendon reflexes. Except for slight mental dulling there was no psychologic abnormality. Rare observations were trophic and sphincter disturbances. Sensory loss and ataxia were slight as compared with observations on adults. No cases of "crises" were encountered.

Twelve cases of congenital taboparesis were studied. There appeared to be definite intermediate cases approaching dementia paralytica on the one side and tabes dorsalis on the other.

The following observations were based on sixteen cases of congenital dementia paralytica. Diagnosis of this condition rests on various criteria: neurologic psychic, serologic and pathologic. All four criteria are not always present and as a result the personal element enters prominently into making the diagnosis.

The age of onset average 13 years (extremes, 6 and 16 years). There was intellectual backwardness together with certain infantilism. The onset was usually gradual. The quantitative defect in the intellectual sphere ranged from mere childishness to a complete dementia with disorientation, confusion and loss of sphincter control. Hallucinations, illusions and delusions may occur but were rarer than in the adult. Speech defects were extremely common and important. Frequent observations were: tremor of the hands, face, tongue, lips and at times of the legs and the jaw, pupillary abnormalities, optic atrophy, contraction in the arms and legs and early symptoms of the bladder.

LANGMANN, New York.

A CRITICAL EXAMINATION OF THE LANCASHIRE REPORT ON "THE FATE OF YOUNG CHILDREN IN TUBERCULOUS HOUSEHOLDS." H. MIDGLEY TURNER, Tubercle **11**:145 (Jan.) 1930.

Turner finds it difficult to correlate with clinical experience the statement made in the Lancashire report (*Tubercle* **10**:497, 1929; abstr., AM. J. DIS. CHILD. **39**:630 [March] 1930) that the death rate from all causes in the first year of life among children born into tuberculous households was less than the control rate, and the conclusion "that the children in tuberculous households do not suffer in the first five years of life, a death-rate from all causes significantly different from the normal." He bases his criticism on the methods by which the "sample" households were selected. Judged by the report and by his own experience as medical officer (tuberculosis), he feels that the method of selecting sample households was unwittingly faulty and failed largely to include the families of the lower classes, among whom the mortality from tuberculosis is greatest.

SMITH, Ogden, Utah.

THE EFFECT OF DEEP X-RAY THERAPY ON CERTAIN FORMS OF PULMONARY TUBERCULOSIS IN CHILDHOOD. ZOLTÁN VON BÓKAY, Jahrb. f. Kinderh. **123**:18 (Feb.) 1929.

Von Bókay states that certain cases of tuberculosis in childhood may be rapidly healed by deep roentgen therapy (from 20 to 50 per cent) of the skin unit dose, 3 mm. aluminum filter, 30 cm. distance, 100,000 volts, bilateral exposure over the entire surface of the thorax. In most instances, three radiations at monthly intervals are sufficient. The indications for therapy at present are "hilus processes" and "smaller infiltrations."

A. F. ABT, Chicago.

CHANGES IN THE SPINAL FLUID IN TUBERCULOUS MENINGITIS. J. GELDRICH, Jahrb. f. Kinderh. **124**:159 (June) 1929.

Geldrich states that in tuberculous meningitis, even in earliest infancy, the amount of sugar in the spinal fluid diminishes from the normal values of from 50 to 70 mg. per hundred cubic centimeters to from 20 to 30 mg. In the end-stages in exceptional cases the values may again approach normal. A single determination in these instances must be cautiously interpreted. Generally, however, the diminution of the amount of sugar is as characteristic of tuberculous meningitis as is the increase in lactic acid. The latter increases until the end of the illness and may reach ten times the normal value. The sum of the values for sugar and lactic acid in the cerebrospinal fluid is constant, with the exception of the second stage, varying between 70 and 90 mg. per hundred cubic centimeters. The increase in the amount of lactic acid and the decrease in the sugar value may explain the breaking down of the latter. Contrary to previous reports, the author finds that the cerebrospinal fluid becomes more acid as the disease progresses, as determined by electrometrical measurements. Determinations of the p_H of 7.22 or even 7.08 are recorded.

A. F. ABT, Chicago.

PSEUDOPOSITIVE WASSERMANN REACTIONS IN THE FIRST DAYS OF LIFE. L. LEMEŽ, Ztschr. f. Kinderh. **48**:97, 1929.

In 271 newly born babies, the Wassermann test was performed 708 times on the umbilical and on the heel blood; the Sachs-Georgi precipitation test 311 times, Meinicke's cloud test 388 times and Mueller's clumping test 344 times. In most cases the blood was examined at least on the third day, in many cases on the fourth day and sometimes only on the second day of life. The Wassermann reaction of blood from the heel was positive in 18 per cent of 271 new-born infants—in 27.5 per cent if the self-inhibitory reactions are included. Ninety per cent of all self-inhibitory reactions of blood from the heel came on the first three days of life. The remaining 10 per cent was distributed from the fourth to the seventh day. There existed a certain relation between the Wassermann reaction and the birth weight; 21 per cent of newly born infants with poor birth weight and 40 per cent with a good birth weight showed positive reactions. The greatest percentage of positive Wassermann reactions occurred in the first hours of life, on the first, second, fourth and eighth days. The reactions were almost by rule negative for the third to the fifth day, and were to be valued, therefore, as unspecific. As the principal cause for pseudopositive Wassermann reactions was the increased instability of the serum which is expressed, according to Duzar, in a rapid diminution of the serum globulin and of the positive Bárány's reaction during the first ten days of life. But there was the possibility that the instability of the serum was caused or increased partly by allergic processes in the sense of Mayerhofer, that is, caused by protein-like toxins of pregnancy and placental substances. Infants that are free from syphilis as well as those that have congenital syphilis may show unspecific Wassermann reactions in the first two weeks of life. Healthy, newly born babies of syphilitic mothers who showed transiently a positive Wassermann reaction were nevertheless to be considered free from

syphilis so far as they remained clinically healthy and gave a negative Wassermann reaction. The desultory condition of the Wassermann reaction in congenital syphilis is caused by the fact that at first unspecific and later specific reactions occur. As a result of the great number of unspecific reactions, the Wassermann reaction on the first eight days of life cannot be relied on for the diagnosis of syphilis, but a positive reaction the second week of life is always suspicious. The Sachs-Georgi test gave exceedingly few unspecific reactions (0.6 per cent) in the umbilical blood as well as in the heel blood.

Meinicke's cloud test gave 1.7 per cent unspecific results in the umbilical blood but was little reliable for the diagnosis of syphilis. In the heel blood it gave few unspecific reactions (2 per cent), and it appeared in sensitiveness to stand below the Sachs-Georgi test. Mueller's clumping reaction was 27.8 per cent positive in umbilical blood and 33 per cent positive in blood from the heel. The occurrence of positive reactions in umbilical blood was raised as the birth weight increased. In blood from the heel of newly born infants, from 38 to 58 per cent positive reactions were obtained on different days of life. There was no close relation between the Wassermann reaction and Mueller's reaction. As a result of the great number of unspecific reactions, for the most part of the second but also of the third and fourth grades, Mueller's reaction was not reliable for the diagnosis of syphilis of the newly born. In the first eight days of life, the Sachs-Georgi precipitation reaction and Meinicke's cloud reaction are especially reliable. The aim of the experiment was to test the Wassermann reaction in newly born infants as to its reliability. On account of the characteristic misleading condition of the Wassermann reaction in the first days of life, one should spare newly born infants this procedure. Between erythema toxicum neonatorum and the number of births there was no relation. The casual relation between syphilis and hydrocele, without and partly with specific disease of the testis, was denied, since every third newly born infant had a nonsyphilitic hydrocele which according to Mayerhofer is to be looked on like other allergic pregnancy reactions. Enlargement of the spleen in newly born infants in the first fourteen days of life was neither typical nor reliable as a sign of congenital syphilis, since straight syphilitic newly born infants do not always or only seldom show an enlarged spleen. On the other hand, one finds in almost three-fourths of syphilis-free newly born infants a considerably enlarged spleen which is the result of an allergic leukopenia. Newly born infants often have rhinitis in the first hours of life as a result of the prophylactic use of silver in the eyes. The nasal mucous membrane reacts with catarrhal swelling; sometimes with exudation. The recognition of this silver rhinitis is important for the differential diagnosis of syphilitic coryza. Like the pseudopositive Wassermann reaction, the swelling of the peripheral lymph glands, the enlargement of the spleen and the hydrocele, silver rhinitis counts as a pseudosyphilitic sign.

EMERSON, Boston.

THE CONDITION OF THE CAPILLARIES AND THROMBOCYTES IN CHILDREN WHO HAVE TUBERCULOSIS, ESPECIALLY THOSE WITH PURPURA. M. GIUFFRÉ, Ztschr. f. Kinderh. **48**:177, 1929.

For the pathogenesis of the purpura that occurs occasionally in tuberculosis there is greater interest in the study of the blood capillaries, capillaroscopy and the testing of capillary resistance than in the counting of platelets. In the cases beyond question the number of platelets is normal or increased as is usual in the fever-free periods in tuberculosis. One could assume a functional inferior quality of the platelets in the sense of Glanzmann (thrombasthenia), but there is no diminution of the platelets as usually occurs during fever, accompanied by hemorrhagic purpura. The testing of capillary resistance reveals an increased quality of breaking, many times over the entire skin but frequently limited to the sites of hemorrhages and to the lower extremities. The skin capillaries showed changes of circumference and form which were visible in the neighborhood of the

hemorrhages. In cases which showed no purpura there was often a diminution of capillary resistance, which signifies that this diminution is not the only factor even if it is one of the most important in the pathogenesis of purpura. One must not forget that mechanical factors (changes in capillary pressure and in the velocity of the blood), conditions in the plasma (physical, chemical and physicochemical changes), conditions in the bone-marrow, which may be associated with changes in the formed elements of the blood and especially of the platelets, and conditions in the vessel endothelium (changes of the capillary picture and of capillary resistance) are mingled in each case of secondary purpura in different measure and manner. The same mesenchymal origin of the blood capillary and the hematopoietic organs make the assumption probable that both suffer changes at the same time, either under the direct injurious influence of the toxin of tuberculosis or indirectly by way of an impairment of the function of the glands of inner secretion.

EMERSON, Boston.

THE QUESTION OF THE COMPLETE HEALING OF TUBERCULOSIS IN CHILDHOOD. E. NOBEL and R. SEIDMANN, Ztschr. f. Kinderh. **48**:226, 1929.

The question of complete biologic cure of an infection with tuberculosis in children was studied by means of the tuberculin reaction. Fifty patients having different lesions, tuberculous and nontuberculous, who had had a positive Pirquet reaction, were retested from four to seventeen years afterward. Forty-nine patients reacted positively; forty-five of them after the first test, 4 only after 0.1 mg. of intracutaneous tuberculin. Only one child, aged 8¼ years, who was positive four years before, and who showed by roentgen examination a definite primary focus (Ghon) and the primary complex of Ranke, was negative to 100 mg. of old tuberculin. It was assumed here that no immunity against tuberculosis existed, while the forty-nine other cases bore out the assumption that because of the lasting presence of virulent bacilli which the new positive test showed, the first infection with tuberculosis yielded the basis for later immunity. The complete biologic healing of the first infection with tuberculosis is most infrequent.

EMERSON, Boston.

Internal Diseases

SICKLE CELL ANEMIA. B. STEINBERG, Arch. Path. **9**:876 (April) 1930.

This is a review of the historical, theoretical, and clinical aspects of sickle cell anemia. The association of the sickling phenomenon and anemia was first pointed out by Herrick in 1910. For many years the condition was thought to occur only in the colored race, but in the last few years several cases have been described in white persons. Among the theories that have been advanced to explain the condition, that of Hahn and Gillespie is of interest. In their opinion, anoxemia is a factor. They produced sickling experimentally by reducing oxygen tension, and then restored the cells to their normal shape again by raising the oxygen tension. The increase in sickling in sealed fresh preparations at 37 C. might fit in with this idea. It is pointed out that sickling may be present without any clinical manifestations of disease. The gross and microscopic pathology of the condition is discussed in detail. Splenectomy and transfusions of blood have met with little success; better results have been reported with a liver diet. Death usually occurs from some intercurrent disease. The prevailing conception is that sickle cell anemia in itself is not fatal.

LESLIE, Evanston, Ill.

OSTEOGENESIS IMPERFECTA CONGENITA. M. WEBER, Arch. Path. **9**:984 (May) 1930.

The insight into the problem of osteogenesis imperfecta, herein presented, is based on the author's thorough understanding of the various stages in the histologic

morphology of bone production. In the case studied, which was that of an infant aged 2 days, the highest stage of bone formation, i. e., the lamellar or shell bone, was completely lacking, as was also the process of resorption by osteoclasts. The conclusion drawn is that in osteogenesis imperfecta the entire bone system has been arrested in the stage of nucleus formation. All the bone present consists of fiber bone. Either the osteoblasts are lacking or they do not carry on their destined function. The fractures, though characteristic of the condition, are secondary. The question as to the cause remains unanswered. Is there a germinal (vitium primal forationis) lack, or is the disturbance secondary? The article is illustrated.

LESLIE, Evanston, Ill.

THE THYMUS GLAND IN LYMPHATIC LEUKEMIA. H. M. MARGOLIS, Arch. Path. **9**:1015 (May) 1930.

The thymus gland was studied in thirty-two cases of lymphatic leukemia. In only four cases was there any enlargement of the gland, and in these the changes were due to infiltration with lymphocytes similar to that found in nonlymphatic organs. In the remaining cases the gland showed either no abnormality or varying degrees of involution. The reaction of the small thymic cells in lymphatic leukemia differs, then, from that of the blood lymphocytes, and suggests that these two types of cells, although similar morphologically, have a different histogenetic source.

LESLIE, Evanston, Ill.

ADIPOSOGENITAL DYSTROPHY WITH RETINITIS, MENTAL DEFECT AND POLYDACTYLISM (LAURENCE-MOON-BIEDL SYNDROME). H. LISSER, Endocrinology **13**:533, 1930.

An instance of this rare condition is described clinically in a girl 8 years old.

[ARCH. PATH.].

THE PROBLEM OF CHRONIC ANOREXIA IN CHILDHOOD. F. W. SCHLUTZ, J. A. M. A. **94**:73 (Jan. 11) 1930.

Chronic anorexia is seldom encountered in a child with rugged physique but in the thin, pale, underweight child who is functionally below par, that is, the hyposthenic or asthenic type in whom there is a general lack of muscular tone of all structures including the gastro-intestinal tract. It may develop in two ways: either as a constitutional disposition or as the result of the prolonged action of some disease process or focus. These children are frequently the offspring of intellectual persons who themselves are of this type and who furnish the worst possible association for the child already handicapped by this vicious constitutional disposition. These children have been shown to have a marked decrease in gastric motility, which is greatly aggravated by emotional factors and environmental influences. It is the author's impression that the environment of the child is probably the greatest factor in the development of anorexia and creates the most difficult problem in successful management of the condition. The environmental factor should be the first to be considered in the treatment for this condition. The food should be selected with reference to high mineral, vitamin and carbohydrate content, with great concentration, small volume and low fat value. The excessive consumption of cow's milk is not good for the child with anorexia, although it is always readily taken. Removal of this article of food from the diet often results in improvement. The selection of food should at no time be left to the inclination and choice of the child. A complete rest period of not less than two hours, preferably in the afternoon, is important. Frequently half day school must be resorted to. Medicinally, diluted hydrochloric acid seems indicated. The liberal use of cod liver oil and some form of heliotherapy is beneficial.

BONAR, Salt Lake City.

CAUSES OF FAILURE IN THE TREATMENT OF DIABETES IN CHILDREN. FRANK N. ALLEN and RUSSELL M. WILDER, J. A. M. A. **94**:147 (Jan. 18) 1930.

In an analysis of a group of fatalities from diabetes in childhood the following rules have been suggested: (1) Provision of a diet which satisfies the child and keeps it in good nutritional condition; (2) maintenance of a balance between the dosage of insulin and the diet, increasing the insulin on the appearance of glycemia, and decreasing it on the occurrence of symptoms of hypoglycemia; (3) urinalyses morning and evening, so that a decrease in tolerance can be recognized and combated by an increase in the dosage of insulin; (4) checking of each new supply of Benedict's quantitative solution by tests with corn syrup or honey; (5) tests of urine at least four times daily during acute illness; (6) on the development of acidosis, frequently repeated doses of insulin are given after tests of the urine or blood; (7) consideration of juvenile diabetes as potentially severe in all cases; (8) administration of insulin, and (9) continuous supervision.

BONAR, Salt Lake City.

THE ANTIEDEMIC ACTIONS OF CALCIUM IN EXPERIMENTAL IRRITATIVE EDEMAS. M. L. TAINTER and WILLIAM VAN DEVENTER, J. A. M. A. **94**:546 (Feb. 22) 1930.

The alleged specific antiedemic action of calcium lacks a satisfactory experimental basis, and the theoretical antipermeability effect of calcium on tissues and organs in situ lacks convincing evidence, according to the authors' experiments with the irritative edemas. They seriously doubt the therapeutic usefulness of calcium in clinical irritative edemas.

BONAR, Salt Lake City.

UREMIA IN CHILDREN. JOSEPH K. CALVIN, M. Clin. North America **13**:1211 (March) 1930.

Two types of uremia are described in this paper: acute convulsive uremia and true chronic uremia. The former commonly occurs during an attack of acute hemorrhagic nephritis. It is characterized by acute onset, edema, convulsions, rapidly increasing arterial hypertension and suppression or anuria. The blood shows only moderate retention of urea and nonprotein nitrogen, and moderate lowering of the carbon dioxide-combining power. In combating this condition, the following measures are effective: lumbar puncture, with venesection when arterial pressure is very high; elevation of the head, and intravenous injection of 20 per cent dextrose and 2 per cent magnesium sulphate, administered very slowly, to relieve cerebral edema, reduce blood pressure and control convulsions. Fluids should be given by every possible avenue. Morphine combined with 25 per cent magnesium sulphate given subcutaneously is of value. After the cessation of vomiting, magnesium sulphate is given daily by stomach tube if necessary, until the blood pressure remains under 110. Dry heat is effective in bringing about the elimination of water and urea. When the acute uremic stage is under control, the underlying acute hemorrhagic nephritis requires careful management. Rest in bed is essential until the edema has disappeared and the blood pressure and urine are normal. Proteins and salts are reduced in the diet to lessen the work of the kidneys. During convalescence the amount of fluids to be administered should be gaged by the patient's ability to excrete urine. Intramuscular injections of whole blood are of value in combating anemia and probably serve to increase the patient's resistence to toxic agents. Permanent cure may be anticipated in most patients who have been properly treated.

True chronic uremia is the terminal stage of chronic progressive glomerular or interstitial nephritis, and is not curable, although progress may at times be checked for short periods. Its onset is insidious and usually without convulsions. Arterial tension may or may not be increased. Air hunger is marked. The carbon dioxide combining power of the blood is markedly decreased, and there

is marked retention of urea and nonprotein nitrogen. The same general line of treatment indicated for the convulsive type may be tried, without hope, however, of permanent benefit.

SMITH, Ogden, Utah.

HYPERTROPHIC PYLORIC STENOSIS IN COLORED INFANTS. M. GLEICH and S. GOODMAN, New York State J. Med. **30**:140 (Feb. 1) 1930.

Hypertrophic pyloric stenosis is rare in colored infants. Two typical cases of this condition are reported, one in a patient aged 5 weeks and the other in one aged 22 days. Both recovered after the Fredet-Ramstedt operation.

AIKMAN, Rochester, N. Y.

PARADOXICAL EMBOLISM. THEODORE THOMPSON and WILLIAM EVANS, Quart. J. Med. **23**:135 (Jan.) 1930.

The authors define the condition known as "crossed" or "paradoxic embolism" and review the cases reported in the literature. Reference is made to the site of the embolism, and the incidence and degree of patency of the foramen ovale are discussed. The relationship between paradoxic embolism and pulmonary embolism is discussed, and emphasis is given to the difficulty experienced in the diagnosis of the condition during life.

The authors state that it is justifiable to assume that the embolism is of the paradoxic type when a patient with venous thrombosis develops cerebral embolism, or more rarely embolism involving an artery to one of the limbs, especially if the patient reveals no clinical evidence of any other cardiovascular disease. Should the embolism be preceded by the occurrence of pulmonary infarction, the diagnosis becomes more certain.

BRADFORD, Rochester, N. Y.

CRITICAL REVIEW: THE LIVER TREATMENT OF ANAEMIAS. JANET M. VAUGHAN, Quart. J. Med. **23**:213 (Jan.) 1930.

Literature relative to the subject of liver therapy in the various types of anemia is reviewed:

The author concludes that liver is a certain remedy in forms of anemia characterized by megaloblastic hyperplasia of the bone-marrow, i. e., in pernicious anemia, sprue and the pernicious anemia of pregnancy. It is also of definite value in some cases of anemia secondary to gastric hemorrhage and in the nutritional type. In other forms it is of little value. It is believed that the action of liver is dependent on at least two distinct factors: its inorganic salt content and the complex polypeptide isolated by Cohn, Minot, Allies and Salter.

The author concludes that pernicious anemia must be recognized as a deficiency disease, in which the bone-marrow is unable to produce its normal quota of red blood cells owing to the absence of some principle present in the liver and kidney.

In patients suffering from pernicious anemia, sudden improvement in the mental state and rapid gain in weight are as characteristic as is the rise in the reticulocyte count following the administration of liver. The leukopenia is not invariably lost as a result of liver treatment. The claim that eosinophilia is characteristic of the response to liver appears to be without satisfactory foundation.

BRADFORD, Rochester, N. Y.

CHANGES IN THE INFANT HEART AFTER IMPROVEMENT OF RESPIRATORY INSUFFICIENCY. DUPASQUIER and DANHIER, Bull. Soc. de pédiat. de Paris **27**:254 (May 21) 1929.

Ten cases of children with respiratory insufficiency were observed. Roentgenograms were made of the heart shadows before and after recovery. These showed some dilatation of the right ventricle which completely disappeared after the

return to normal of the respiratory function. The ventricular index, which according to Duhem normally ranges from 1.25 to 1.30, was always increased (as high as 2.04) when measured on the first examinations and diminished with the return to normal of respiration. The chest expansion and vital capacity also increased in all of the patients observed. The improvement was brought about by giving the children a course in remedial exercises to bring the action of their respiratory muscles up to normal. The right ventricular dilatation is caused by the poor pulmonary circulation resulting from the pulmonary hypofunction and the diminution in thoracic aspiration due to the respiratory movements of poor amplitude.

BENJAMIN, Montreal, Canada.

INTESTINAL INFANTILISM. L. RIBADEAU-DUMAS, R. MATHIEU and WILLEMIN, Bull. Soc. de pédiat. de Paris **27**:257 (May 21) 1929.

Herter's description of the condition as distinguished from "marasmus" is mentioned, and Gee's monograph on celiac disease is referred to. The disease is not common. Still found seventeen cases in the Children's Hospital in London among 14,800 admissions of children under the age of 12 years. The symptoms which these children showed were loss of weight, large distended abdomens and loose, light colored stools. Four patients ranging in age from 7 months to 3 years. None of these patients could walk; all had delayed dentition, and none had signs of rickets. All authors who have studied this disease have reported as the outstanding observations a marked intolerance to fat, a limited tolerance to carbohydrate and a loss of calcium, magnesium and phosphorus in the stools. All recommend the use of a high protein diet; a cow's milk-free diet was advised by Gee. The diet with which improvement was obtained in the patients consisted mainly of animal and vegetable proteins; cream of rice was the best tolerated carbohydrate, and bananas were also well digested. The authors stress the important rôle of mineral salts cod liver oil and ultraviolet irradiation in this disease. In their study of the stools they found an excess of neutral fats, fatty acids and soaps, as well as an increase in the amounts of organic acids and ammonia.

BENJAMIN, Montreal, Canada.

GLYCOGENIC HEPATONEPHROMEGALY. E. VON GIERKE, Beitr. z. path. Anat. u. z. allg. Path. **82**:497, 1929.

Von Gierke presents the case report of a condition which he believes to have no counterpart in the literature. The case is that of a girl who died at the age of 8 years. The family history was negative, and birth and early development had been normal. Unusual prominence of the abdomen had been noted by the family physician at the age of 2 or 3 months and had been present since birth, according to the mother. Throughout its life the child had been susceptible to infections of the upper respiratory tract. She had had a number of attacks of nosebleed, and had been treated for rickets, from which she recovered. The child had been admitted to the hospital when 5 years old. At this time the abdomen was large. The liver was greatly increased in size. There was questionable enlargement of the spleen. There was moderate secondary anemia, with relative lymphocytosis. The suggested clinical diagnosis at this time was Banti's disease. The final admission was for an acute infection of the upper respiratory tract, which resulted in death. At necropsy, the liver weighed 2,000 Gm. instead of 634 Gm. which is the average weight for the age and sex of the patient. The kidney weighed 245 Gm. instead of the average 133 Gm. There was no ascites. The spleen was of normal size and weight. The thymus and suprarenal glands were small. Microscopic examination revealed the presence of moderate amounts of fat in the liver cells. The latter did not give the lipoid reactions of Niemann-Pick disease (lipoid histiocytosis, Bloom). The liver cells were filled with glycogen, as were also the tubular epithelia of the renal cortex. The glycogen could be stained by carmine and gave the iodine reaction. The liver contained 10.43 per

cent of glycogen calculated for moist weight of the tissue, and 33.72 per cent calculated for the dry weight. The kidney contained 6.53 per cent glycogen, moist weight, and 36.82 per cent, dry weight. The glycogen did not disappear from fresh liver tissue kept for six days in the incubator in normal physiologic solution of sodium chloride and chloroform water. The pancreas was histologically normal. After von Gierke had completed the study of his case, he learned of an apparently similar one that had come to necropsy in Vienna in 1928. This case he also presents. The child was a boy, aged 4 years and 10 months. The liver and kidneys were enlarged, and the parenchymatous cells of these organs contained large amounts of glycogen. As a working hypothesis to explain the condition reported, the author postulates a disturbance of intracellular glycogen metabolism, which leads to deposition of the glycogen in the cells of the liver and kidney. Early embryonic tissues, especially liver, kidney and muscle, are rich in glycogen, indicating the early development of the property of intracellular glycogen synthesis. The glycogen store disappears from the tissues at or shortly before birth, indicating a later development of the property of intracellular glycogenolysis. In the condition reported, it is supposed that the cells of the liver and kidney failed to develop the normal property of splitting glycogen.

SCHULTZ, Chicago.

LYMPHOGRANULOMA IN CHILDREN. WALDEMAR FEER, Jahrb. f. Kinderh. **123**: 145 (March) 1929.

Feer reports nine cases of lymphogranuloma in children. Seven of these patients gave negative reactions to the tuberculin test and at autopsy were found free from tuberculosis. In one instance in which there was a positive Pirquet reaction, tuberculin anergy later set in. Observations on young children indicate that there is no question of tuberculosis as an etiologic factor. Lymphogranulomatosis must be considered as an infection *sui generis* with an unknown exciting cause.

A biopsy is necessary to substantiate the diagnosis. Males are affected four times as often as females. The best treatment is roentgen radiation, which should be administered as soon as possible, with high dosage at short intervals. The shortest duration of illness was two months, the longest nine years. One of the patients was free from recurrence and clinically well six years later, but Feer does not maintain that there is complete clinical and anatomic cure.

A. F. ABT, Chicago.

LIPOID CELL SPLENOHEPATOMEGALY. G. DIENST, Jahrb. f. Kinderh. **123**:181 (March) 1929.

According to Dienst, in lipoid cell splenohepatomegaly one is dealing with a congenital, familial, constitutional systemic disease of infancy which manifests itself by a disturbance in the lipoid metabolism and a deposition of lipoids in the cells of the reticulo-endothelial system. According to the morphology of the cells, one distinguishes anatomically between the Gaucher and the Niemann-Pick types. The etiology and pathogenesis are as yet unknown. There is no satisfactory therapy. All of the patients in the case hitherto reported died during the first two years of life.

A. F. ABT, Chicago.

ROENTGEN THERAPY OF SPASTIC COUGH AND ITS INFLUENCE ON THE HEMOGRAM. K. SCHRUTZ and O. VYCHYTIL, Jahrb. f. Kinderh. **123**:200 (March) 1929.

Schrutz and Vychytil state that the enlargement of the intrathoracic glands in pertussis is an important factor in the mechanism of spastic cough. The degree of glandular enlargement may be indicated by considering the general condition of the child and the number and intensity of the attacks. In neuropathic children

one may find only a slight glandular enlargement, in spite of intense spasmodic cough.

Roentgen radiation induces a diminution in the size of the lymph glands and a cessation in the pressure on the bifurcation which causes the spasmodic attacks.

One treatment is given, consisting of from 35 to 50 per cent of the adult skin unit dose on a ventral or dorsal field from 6 by 8 cm to 8 by 10 cm. at from 25 to 30 cm. focal distance, hard rays 130 kilovolts for five minutes, with an aluminum or a 0.5 mm. copper filter. The lymphocytosis soon disappears.

The lymphocytosis is said to be induced in part by the mechanical expression of the lymphnodes in the process of coughing. In tuberculous broncho-adenopathy with and without complicating pertussis, similarly good results may be obtained by radiation or x-ray therapy.

A. F. Abt, Chicago.

Pulmonary Infarcts in Children. H. Schadow, Jahrb. f. Kinderh. **123**:272 (April) 1929.

In recent years there has been an increase in the reports of pulmonary emboli and pulmonary infarcts in children. Schadow reports thirteen cases observed by himself.

The source of embolus was omphalitis, sinus thrombosis in marasmus, infectious diseases and otitis. In 80 per cent of the cases there was found not only pulmonary embolus but also infarct (Lubarsch found 30 per cent in adults). Simple infarcts are not so infrequent even in septic processes, even in endocarditis lenta.

The differential diagnosis from bronchopneumonia is often impossible. In the presence of suitable etiologic factors and sudden onset of pulmonary symptoms, embolism and infarct should be considered.

The prognosis is usually serious in view of the serious character of the etiologic factors, although infarcts may be cured by resorption.

A. F. Abt, Chicago.

The Relationship Between Acrodynia and Miliary Fever. T. Zechlin, Jahrb. f. Kinderh. **124**:195 (June) 1929.

Zechlin minutely reviews the history, epidemiology and symptomatology of acrodynia and miliary fever. He finds that there is much in common in the distribution and clinical manifestations of these two diseases. He points out that they are both of unknown etiology, and that in both the central nervous system is early affected. In conclusion he presents a summary of all of the cases of acrodynia that have occurred in Germany.

A. F. Abt, Chicago.

Treatment for Congenital Myxedema with Thyroxin. E. Nobel and W. Kornfeld, Ztschr. f. Kinderh. **48**:216, 1929.

A girl, aged 17, who was previously untreated for severe congenital myxedema, was given thyroxin for one and one-half years. She grew 18 cm. in height and overcame her great retardation in bone development. Especially rapid were the specific changes in the soft parts. The mental growth was less satisfactory because of the long period without treatment.

Emerson, Boston.

The Pathogenesis of Acetonemic Vomiting of Children. Walter Heymann, Ztschr. f. Kinderh. **48**:230, 1929.

Examination of the blood in a case of acetonemic vomiting gave the following results: normal blood sugar in the attack, no real disturbance in the glycemic reaction after an oral test with dextrose on well days and stronger and longer continued hyperglycemia with epinephrine in an attack produced in a child used as a control by the withdrawal of carbohydrate. The hypotheses held up to the present time, the theory of "glycogen storage," after due consideration, are rejected.

The similarity of the disease, clinically and pathogenetically, to hyperemesis gravidarum and the advantage arising from it for the further study of the problem are emphasized.

EMERSON, Boston.

A CASE OF GONORRHEAL EPIDIDYMITIS AND OMPHALITIS IN AN INFANT AGED THREE MONTHS. K. WIESNER, Ztschr. f. Kinderh. **48**:305, 1929.

Besides this case of epididymitis in an infant, there are only two others reported in the literature. The mother had gonorrhea, and it was thought that she gave the infant the infection while taking care of him.

EMERSON, Boston.

Nervous Diseases

THE DEVELOPMENT OF THE PLANTAR REFLEX IN CHILDREN. RAYMOND W. WAGGONER and WILLIAM G. FERGUSON, Arch. Neurol. & Psychiat. **23**:619 (April) 1930.

A careful, extensive investigation of the Babinski sign in normal infants is reported. In a determination of the plantar reaction, the intensity of the stimulus is important since it is a skin reflex. If the stimulus is too strong there is apt to be a reversal of the reaction to flexion. The reaction may be reversed by sleep. At the age of 1 year the reaction has become almost entirely that of adult flexion.

BEVERLY, Chicago.

ACUTE TOXIC (NONSUPPURATIVE) ENCEPHALITIS IN CHILDREN. A. A. LOW, Arch. Neurol. & Psychiat. **23**:696 (April) 1930.

The author gives a detailed pathologic report of five cases of toxic encephalitis. He further establishes toxic encephalitis as a definite pathologic entity. He concludes that there are two types of toxic encephalitis, one with peracute liquefaction and predominately regressive glial changes, especially of the cortex, and another with acute liquefaction and predominately progressive glial changes. Peracuteness or acuteness of the process depends largely on the virulence of the toxin.

BEVERLY, Chicago.

EPILEPSY: EVIDENCES OF BODY FLUID VOLUME DISTURBANCE. JAMES L. GAMBLE, Arch. Neurol. & Psychiat. **23**:915 (May) 1930.

This is a study of body fluid disturbance (water storage) in epilepsy. By determining the fixed base excreted in the urine, it was demonstrated that water storage occurs between the attacks and that this is followed by a release of body fluids immediately following an attack.

BEVERLY, Chicago.

THE THERAPEUTIC EFFECT OF DEHYDRATION ON EPILEPTIC PATIENTS. TEMPLE FAY, Arch. Neurol. & Psychiat. **23**:920 (May) 1930.

The author reviews the literature and discusses fully from the theoretical and practical standpoints the subject of dehydration and its relationship to epilepsy. It also includes a summary with case illustrations of his treatment for epilepsy by this method. Dehydration is demonstrated as a valuable adjunct in the control of major convulsive seizures. The seizures return when the dehydration is discontinued.

BEVERLY, Chicago.

SERUM MENINGITIS. D. GOLDMAN, Arch. Path. **9**:1027 (May) 1930.

After a review of the literature on aseptic meningitis, the author reports results obtained in dogs following the injection of various substances into the cisterna. A marked increase in cell count and the histologic picture of meningitis resulted from the injection of horse serum, antimeningitis serum, antitetanus serum, salt solution and 0.4 per cent cresol. When spinal fluid was injected there was a transient increase in cells but no observable histologic change in the meninges. The aseptic meningitis is of short duration and produces no permanent changes in the meninges or nervous system. These observations should be kept in mind in such diseases as tetanus and in diseases with meningeal symptoms but without actual meningitis. In such cases large intrathecal injections might lead to confusion in diagnosis or result in actual harm to the patient.

LESLIE, Evanston, Ill.

PAPILLOMAS OF THE CHOROID PLEXUS. WILLIAM P. VAN WAGENEN, Arch. Surg. **20**:199 (Feb.) 1930.

Two cases of true papilloma of the choroid plexus of the left lateral ventricle are reported. One, in the case of an infant, aged 3 months, was uncovered at an operation, treated with deep roentgen therapy and later removed in toto at a second stage operation. In the second case the tumor was encountered at autopsy; it showed one large growth with numerous small papillomas "seeded" throughout a portion of the ventricular system. The choroid plexus in the right ventricle was normal. Not only the author's case but some five or six other cases in the literature are examples of "seeding" of choroid plexus papillomas. This, van Wagenen considers not as an evidence of malignancy of the tumor, but rather as a probable accidental occurrence in which trauma may have played a considerable part.

A review of the literature revealed about forty-five cases; from them the author found that the favorite site for these tumors is in the fourth ventricle where 50 per cent of the recorded cases were found; 34.7 per cent were in the lateral ventricles, and 17.3 per cent in the third ventricle. By some curious coincidence, 93 per cent of tumors of the lateral ventricle have been found on the left side. Van Wagenen also found that the age incidence was greatest in the first decade and gradually diminished up to the sixth decade.

MASSON, New York.

THE ETIOLOGY OF INFANTILE SPASMOPHILIA. H. J. GERSTENBERGER, J. I. HARTMAN, G. R. RUSSELL and T. S. WILDER, J. A. M. A. **94**:523 (Feb. 22) 1930.

The authors have presented additional evidence that three factors are essential to the development of infantile spasmophilia: rickets, exposure of the rachitic infant to the influence of the antirachitic factor in one form or another in a sufficient degree to produce healing, and interruption or inadequacy of the exposure. The evidence presented consists of the report of the development of spasmophilia due to interrupted therapy in two rachitic infants and due to inadequate therapy in one rachitic infant.

BONAR, Salt Lake City.

POLIOMYELITIS. ROBERT H. RILEY, J. A. M. A. **94**:550 (Feb. 22) 1930.

A plea is made to the medical profession for early diagnosis, observation, early serum treatment and after-care in poliomyelitis. The diagnosis before paralysis is important. The appearance of prostration out of proportion to the temperature, a flushed face and anxious expression, mild infection of the throat, rapid pulse, a coarse tremor on movement, the head tilted on the neck, stiffness of the spine, pain on anterior flexion and an increase in the cellular and globular contents of the spinal fluid is indicative of poliomyelitis, and the serum of convalescent

patients should be administered. Early repeated spinal drainage and the use of the serum of convalescent patients are most important in the preparalytic stage of the disease. The treatment for this disease under proper conditions and by competent persons reveals that between 70 and 80 per cent of the patients showed good recovery as compared with 20 per cent who received less intensive treatment.

BONAR, Salt Lake City.

THE TREATMENT OF EPIDEMIC MENINGITIS. J. B. NEAL, New York State J. Med. **30**:79 (Jan. 15) 1930.

Intensive methods of treatment by combined intraspinal, intravenous and intramuscular injections of antimeningococcic serum have never impressed favorably the Meningitis Division of the Research Laboratory of the New York City Health Department, of which the author is a member. In nineteen years the division has supervised the care of more than 1,000 cases of epidemic meningitis. The results were compared with those of a "children's service in an excellent hospital in New York City." Seventy-nine patients were treated in this hospital from January, 1918, to October, 1921, by the more intensive methods, with a mortality of 54 per cent. During the same period the Health Bureau treated 254 patients conservatively, with a mortality of 23 per cent.

Patients are treated as follows: Whenever a cloudy fluid is found, serum is immediately administered. Intraspinal injections are given daily in amounts of 20 cc., if possible, until at least two successive fluids show no organisms by smear or culture. The cell count is of itself of little value since the prognosis is poor if the fluid becomes clear and the organisms persist.

A return to normal of spinal fluid sugar is a good guide. It is desirable to drain the subarachnoid space as completely as possible, but it should be done slowly and carefully, especially if the fluid is under great pressure. Occasionally from 50 to 60 cc. may be safely withdrawn. When large amounts are obtained, more serum may be given. Graduated doses are not used for small children. The dosage given depends on the amount of fluid withdrawn and the ease with which serum runs in by gravity. The only condition for which spinal puncture is made and serum is given more often than every twenty-four hours is greatly increased pressure.

At least four doses are usually required. The average patient receives from six to eight doses and occasionally twelve. If the symptoms do not improve after two sterile fluids have been obtained, more serum is given.

The author prefers ventricular taps to cisternal punctures in blocked cases. While she has seen no immediate harm from ventricular punctures, she knows that death from hemorrhage has occasionally followed cisternal puncture.

Intravenous or intramuscular injections are used only in cases of meningococcic septicemia or in cases of meningitis with positive blood culture or a rash that tends to persist or recur. Intravenous injections are more apt to give severe reactions. The serum produced by the New York State Health Department has been most satisfactory.

AIKMAN, Rochester, N. Y.

HYSTERIA IN CHILDREN. G. HEUYER, Bull. Soc. de pédiat. de Paris **27**:244 (May 21) 1929.

Hysteria in children is rare. The case is cited of a child in whom mutism came on for no apparent reason and lasted four months. The mutism disappeared six weeks after treatment by psychoanalysis was begun. The child had been subject to convulsions and was somewhat feebleminded. Although no physical signs of organic disease were found, the author is not sure that this was a case of real hysteria. He also cites the case of a girl who had a peculiar spasmodic cough. Psychoanalysis revealed that she was jealous of her sister. She had had a friend who died of tuberculosis, and, wishing death on herself, she began to

cough, believing that she had tuberculosis and would die. She was cured by psychoanalysis. Later the cough returned and another physician gave her one injection of pilocarpine, after which she stopped coughing. No signs of any organic disease were found in this child, but the author does not feel certain that she presented a case of true hysteria. He agrees with Dejerine, who thinks that hysteria does not occur in the child. In true hysteria there must be an imaginary mental basis of which mythomania is one aspect and autosuggestion or heterosuggestion is another, and there must also be a particular psychoplasticity which permits the patient to reproduce an organic syndrome without presenting any physical signs of organic disease; in reality, these organic syndromes are always incompletely reproduced and show atypical forms which immediately reveal their illegitimacy. In all cases of pseudohysteria there is some painful stimulus against which the child shows a defensive reaction; this is not true hysteria. The author cites examples of this "antalgic attitude."

BENJAMIN, Montreal, Canada.

PUNCTURE ACCORDING TO ANTON AND SCHMIEDEN'S METHOD IN A CASE OF INTRACEREBRAL HYPERTENSION. NAGY, Rev. de chir. (Bucuresti), 1929, no. 8.

In a case of hydrocephalus and intracerebral hypertension due to obstruction of the foramen of Magendie resulting in blockage of the communication between the intracranial and the intraspinal fluid of the subarachnoid spaces, the author recommends the puncture of Schmieden as it is apt to restore the communication. As long ago as 1908 a similar subcerebellar puncture was advocated and carried out by Obreja. He did not, however, transfix the membrana tectoria; he transfixed the membrana cerebellomedullaris which covers the subarachnoid cistern and the subcerebellar space. This subcerebellar puncture lends itself perfectly to diagnostic and therapeutic purposes; its technic is simple, but it requires, of course, skill and caution.

N. BLATT, Siebenbuergen, Roumania.

OCCIPITAL SPINA BIFIDA. M. SALVAT y ESPASA, But. de la Soc. Catalana de pediat. **1**:15 (Jan.) 1928.

A case study is reported in a child, aged 3 months, which is interesting because the hernial tumor (which could be reduced) was so small that it might easily have been overlooked.

WATSON, Chicago.

PSYCHOLOGY IN CHILDREN. J. S. GALANT, Jahrb. f. Kinderh. **122**:356 (Jan.) 1929.

Galant presents some theoretical considerations on the pathogenesis or origin of homosexuality in childhood.

The author also disagrees with Adler's explanation of the psychoses on the basis of the struggle for power. The psychotic child is a degenerative psychopathic type. The psychopathic predisposition combined with the unfavorable external influences of life predisposes to psychoses.

Optimistic views are given as to the management of psychotic children in institutions.

A. F. ABT, Chicago.

ENCEPHALITIS IN THE COURSE OF INFECTIOUS DISEASES IN CHILDHOOD. W. REIMOLD and E. SCHÄDRICH, Jahrb. f. Kinderh. **123**:229 (April) 1929.

Reimold and Schädrich state that the clinical manifestations of nonpurulent encephalitis in the course of measles are manifold. The most prominent symptom in childhood is convulsions. Only after cessation of the general and peripheral symptoms is it possible to see the actual extension of the pathologic process. Psychic disturbances up to the point of actual psychoses are frequent. When the encephalitis arises during the prodromal and exanthematous stage, the prognosis

is always doubtful, and the lethal termination is unavoidable. However, lesions in the postexanthematous stage lead most often to recovery. At autopsy there is a hemorrhagic encephalitis of the cerebrum with irregular location of the foci. Histologic examination shows a predominance of vascular lesions.

In scarlatina the importance of the encephalitic process is overshadowed by the occurrence of other cerebral complications, thrombotic embolic processes which play the predominant rôle. Encephalitis after varicella is a rare complication. Permanent injury is more frequent here, and pure cerebellar syndromes are more frequently observed. Encephalitis occurs more frequently in the course of parotitis epidemica.

The differential diagnosis of the various cerebral complications of whooping cough is particularly difficult. Next to the encephalitis, hemorrhage is the most important manifestation.

In recent years there has been an increase in the frequency of encephalitis complicating acute infections. Further clarification of these problems is to be attained by careful gathering of clinical experiences and comparative histologic and serologic studies based on animal experimentation. It is also important to determine whether the encephalitis is induced by a specific virus.

A. F. Abt, Chicago.

Chvostek's Phenomenon. P. R. van der Elst, Jahrb. f. Kinderh. **123**:288 (April) 1929.

Van der Elst states that Chvostek's sign is a reflex phenomenon which occurs in the area below the zygomatic arch and the effectors of which are the mimetic muscles of the upper lip (lightest grade), the alae nasal, the eyelids and the glabella. The reflex disappears for a short period after the injection of procaine hydrochloride into the maxillary nerve, and is found in 50 per cent of adults and in most neuropathic children. This reflex is sometimes erroneously called the facialis phenomenon. This error is avoided by examining the facial nerve as it comes out in the region of the external auditory canal.

A. F. Abt, Chicago.

Clinical Observations on Convulsions Occurring at the Onset of Acute Illnesses in Childhood. E. Faerber, Jahrb. f. Kinderh. **124**:148 (June) 1929.

The occurrence of convulsions at the onset of acute illness is discussed by Faerber. He finds that these convulsions are unrelated to the first day of the disease, to the stage of the rising temperature, or to an unusually high fever. Febrile or infectious convulsions may occur on the second or third day of the illness, when the fever is only moderately high, or the convulsions may also occur during a remission period. One cannot differentiate these convulsions occurring in acute infections and those occurring in epilepsy. Convulsions at the onset of infection occur especially in those children in whose families all types of eclamptic seizures, including epilepsy, are common. In two of ten children closely observed who had fever convulsions genuine epileptic convulsions developed.

A. F. Abt, Chicago.

A Chemical Study of the Cerebrospinal Fluid. B. Steiner, Jahrb. f. Kinderh. **124**:188 (June) 1929.

The inorganic phosphorus concentration in the cerebrospinal fluid varies between 1.4 and 1.6 mg. per hundred cubic centimeters. In meningitis the values are increased to between 1.7 and 3 mg. per hundred cubic centimeters. In tumor of the brain and in acute encephalitis the inorganic phosphorus concentration is diminished. This is an important observation, because in other conditions the phosphorus concentration remains unchanged.

A. F. Abt, Chicago.

THE FIRST EPIDEMIC OF INFANTILE PARALYSIS IN ROUMANIA. M. MANICATIDE, A. BRÂTESCU and A. RUSESCO, Ztschr. f. Kinderh. **48**:125, 1929.

From June to December, 1927, there were 170 cases in the hospital in the first epidemic of infantile paralysis in Roumania. A number of interesting observations are reported. Fever was sometimes absent; it decreased in the favorable cases but this did not guarantee a favorable outcome; it continued in the unfavorable cases. The Kernig sign was absent in the majority of cases. A distinction could be made between a true Kernig sign and a false one, which is due to pain and stiffness in the neck and lumbar region and which disappears if the child is put in a warm bath. There were ten cases in which the sphincter of the bladder or the rectum was affected. Sometimes there was a sudden rash like a heat rash. The localization of paralysis in the lower extremities is explained by the author by (1) myelinization of the nerve system progressing from above downward, as is seen in the development of the infant who first raises his head, then sits up, etc. The lumbar enlargement is developing with greatest activity at the age when the child is susceptible, and because of this greater activity the susceptibility is increased. (2) On account of the strain and fatigue of this enlargement, when the child is beginning to use his lower extremities, the area is still more susceptible. The abdominal reflex was the skin reflex most often increased, 33 per cent. The neck muscles might be paralyzed early and recover quickly, but when the head could be swung backward, from side to side and forward, the case would have a fatal outcome. The author previously reported a tetrad: a swinging head, stiff neck, negative Kernig's sign and increased patellar reflex. No true cases of cerebral paralysis were found; two cases of hemiplegia turned out to be due to tuberculous meningitis, and all cases thought to be cerebral were syphilitic, tuberculous or bacillary meningitis. The general mortality was 17 per cent. Nineteen patients were treated with convalescent serum of these; two were cured. Twenty-seven patients were treated with Petitt's serum; of these, six were cured. Twenty patients were treated by autohemotherapeusis and three were cured; heterohemotherapeusis did not help. None of these methods was reliable.

EMERSON, Boston.

STUDIES OF EPILEPSY: II. THE RÔLE OF CARBON DIOXIDE. J. TICHA, Časop. lék. česk. **67**:125 (Jan. 20) 1928.

Two cubic centimeters of serum taken from epileptic patients during a convulsion reproduced clonic convulsions in the guinea-pig. Cyanosis is produced by a lack of oxygen rather than by an excess of carbon dioxide. The small amount of serum with which convulsions were produced does not speak for carbon dioxide as the etiologic factor. Also, carbon dioxide acts as a muscle sedative while the agent in epilepsy produces hypertonicity. Asphyxia is produced by a smaller concentration of carbon dioxide than is necessary to produce convulsions. If carbon dioxide is the factor, alkalinization with sodium bicarbonate should have a beneficial effect on epilepsy, but no such effect was noted.

STULIK, Chicago.

STUDIES OF CEREBROSPINAL FLUID IN THE MENINGITIDES, ESPECIALLY IN TUBERCULOUS PATIENTS. J. PROCHAZKA, Časop. lék. česk. **67**:313 (Feb. 26) 1928.

The spinal fluid in various meningitic infections was studied as to pressure, clarity, formation of pellicle, cytology, protein gold reactions, and sugar and chloride content. Case reports are cited to show that none of the foregoing factors can be regarded as pathognomonic, but should be considered with the history, bacteriology and other signs and symptoms in arriving at the final diagnosis.

STULIK, Chicago.

Diseases of the Eye

CONGENITAL COLOBOMA OF THE UPPER EYELID WITH DERMOIDS OF THE CORNEA. W. D. HORNER and F. C. CORDES, Am. J. Ophth. **12**:959 (Dec.) 1929.

The authors refer to the rarity of coloboma of the lid and discuss its appearance and extent, the other congenital defects associated with it and its etiology. Dermoids are also discussed. The case reported occurred in a woman, aged 28. The left upper lid showed a cleft 19 mm. wide and 6.3 mm. deep. Just above the cleft was a mass, evidently a lipoma. There was another beneath the bulbar conjunctiva near the external canthus. The lower limbus was straddled by a dermoid, as was also the temporal limbus, their diameters being 9.5 and 4.7 mm., respectively. These tumors affecting the globe were excised, and a laboratory diagnosis of dermoid was made of these astride the limbus, with aberrant lacrimal gland of the subconjunctival mass.

REESE, Philadelphia.

REPORT OF A CASE OF THORN UNDER THE UPPER LID. M. R. SAWHNEY, Brit. J. Ophth. **14**:115 (March) 1930.

The interest in the case lies in the long period that the foreign body remained under the upper lid without exciting symptoms other than lacrimation and photophobia, and the escape of the cornea from damage.

Five months previously, the child had run a thorn into its eye. There was a slight swelling of the lids, congestion of, and mucopurulent discharge from, the conjunctiva. A mass of granulation tissue, external to the caruncle, sprouted from the conjunctival surface of the lower lid. From this the thorn projected passing under the medial side of the upper lid. It was readily removed and measured about 1 inch in length.

ZENTMAYER, Philadelphia.

THE TREATMENT OF HEMERALOPIA AND KERATOMALACIA BY THE FEEDING OF LIVER. TRANTAS, Arch. d'ophth. **46**:551 (Sept.) 1929.

Thirty years ago the author first reported his successful treatment for hemeralopia and keratomalacia with liver. His subsequent experience with this form of treatment has impressed him with its great superiority over all others. In spite of this, only a few authors have reported its use and not one textbook mentions the use of liver in the treatment for these conditions. The work of Minot and Murphy and the experiments of Whipple offer a possible explanation for its mode of action. The author suggests that this form of treatment can be applied profitably to other ocular conditions. He has already begun to recommend it in cases of retinal hemorrhage in adults and in retinitis pigmentosa.

MARLOW, Syracuse, N. Y.

TRAUMA IN THE GENESIS OF ORBITAL SARCOMA. E. MORETTI, Ann. di ottal. e clin. ocul. **57**:515 (June-July) 1929.

A girl, aged 12, was struck in the eye by a potato. Ten days later a swelling of the upper lid and inner part of the orbit developed, and during two months this increased to the size of a lemon, involving both lids and covering the globe completely. Fever and swelling of the glands suggested an inflammatory process, but puncture allowed the escape of only a small amount of pus and tissue composed chiefly of small round cells, allowing the diagnosis of sarcoma. An attempt to eviscerate the orbit was abandoned because of excessive hemorrhage. Radium had no effect. Death occurred one month later. A statistical study reveals contradictory opinions as to the etiologic importance of trauma in malignant tumors. The author believes that it has not been proved that a single traumatism ever produced a malignant growth, but that it has, in some cases, caused an acceleration in the growth of a previously slow-growing tumor, as doubtless occurred in the present case. (Bibliography.)

GIFFORD, Omaha.

CONGENITAL IRIS ANOMALIES: APLASIA SEMICIRCULAR IRIDIS CIRCUMPUPILLARIS. HANS LIEBITZKY, Arch. f. Augenh. **100-101**:771, 1929.

Two cases are described which show a congenital bilateral crescent-shaped aplasia of the sphincter muscle of the iris. This was associated with a pear-shaped pupil, a lack of development of the pupillary margin and anomalies of the anterior layers of the iris. This forms a typical symptom-complex which seems to be exceptionally rare. The cases that have been reported in the literature are reviewed.

Liebitzky points out that this anomaly is seen almost exclusively in light grayish-blue irides. The lack of development of the pupillary margin can be looked on as an anomalous development of the ectoderm which may progress to an absence of the dilator muscle and an aplasia of the sphincter. With this one sees changes in the mesodermal layers of the iris of varying degree so that the author in inclined to regard the primary cause as a failure of development of the pupillary portion of the pars iridical retinae, secondarily associated with varying degrees of anomalous formation of the anterior mesodermal layers. A third case is reported which showed an anomalous formation of the mesodermal layers with no malformation of the ectodermal derivatives.

ADLER, Philadelphia.

MANIFESTATIONS AND COURSE OF JUVENILE EXUDATIVE MACULAR RETINITIS. PAUL JUNIUS, Ztschr. f. Augenh. **70**:129 (Jan.) 1930.

A descriptive portrayal is given of the degenerative disturbance in the macular region of four cases. The etiology according to the history and clinical observations is variant. Similar retinal disturbances have been reported in the literature, but they have been classified differently. Junius believes that they belong in the group which he describes. The outstanding change seems to be in the vascular bed at the macula. He attributes the destruction of the tissue to an alteration of the metabolism in this area.

YUDKIN, New Haven, Conn.

Diseases of the Ear, Nose and Throat

ACUTE PURULENT OTITIS MEDIA IN CHILDREN. N. W. GABLE, J. Florida M. A. **16**:303 (Jan.) 1930.

The author discusses the bacteriology of otitis media, and suggests as treatment early incision followed by douching every two hours with warm boric or Dobell's solution. He warns against the use of drains.

BIEKER, St. Petersburg, Fla.

FOREIGN BODIES IN THE LOWER AIR PASSAGES: REPORT OF TWO CASES. M. A. LISCHKOFF, J. Florida M. A. **16**:443 (April) 1930.

The author reports two cases of foreign body: One child had a sandspur, and the other some uncooked spaghetti, in a bronchus. Tracheotomy was required, after bronchoscopy in the latter instance. Removal was followed by recovery in both cases.

BIEKER, St. Petersburg, Fla.

EAR INFECTIONS IN BABIES. M. F. JONES and J. M. GERSTLY, New York State J. Med. **30**:1 (Jan. 1) 1930.

More attention should be directed toward the antrum and associated mastoid cells in children less than 2 years of age. Antrotomy is a fairly simple operative procedure in infants under 1 year and 6 months. By means of this operation, many cases of latent mastoiditis, intracranial complications and deafness can be avoided. In a series of 317 cases of mastoiditis, 83.5 were due to *Streptococcus hemolyticus*. Most of the patients with mastoiditis who were operated on were less than 2 years of age.

AIKMAN, Rochester, N. Y.

HEARING OF SCHOOL CHILDREN AS MEASURED BY THE AUDIOMETER AND AS RELATED TO SCHOOL WORK. E. B. STERLING and E. BELL, Pub. Health Rep. **45**:1117 (May 16) 1930.

Seven hundred and ten children, varying in age from 8 to 17 years, were tested. In the actual decrease of hearing, the older children were in the majority. The boys were affected more than the girls. The left ears were uniformly better than the right ones. The group of the lowest intelligence quota was highest in loss of hearing, and the percentage of discharge from one or both ears varied inversely with the grade of hearing.

SANFORD, Chicago.

THE EXTRACTION OF FOREIGN BODIES FROM THE ESOPHAGUS. JEAN GUISEZ, Bull. et mém. Soc. de chir. de Paris **22**:112 (Feb. 21) 1930.

Nine cases are reported in which various foreign bodies were removed from the bronchi. Safety-pins are frequently swallowed by infants, usually with the point up. A device for closing the pin enabled the author to remove fourteen without difficulty. Whatever may be one's attitude toward operation after the foreign body has passed the cardia, removal is always indicated when the object is lodged in the esophagus.

BIEKER, St. Petersburg.

DYSPNEA DUE TO INFLAMED ADENOIDS IN AN INFANT. LOUIS LEROUX, Bull. Soc. de pédiat. de Paris **27**:428 (Oct.) 1929.

An infant, aged 4 months, had fever and marked dyspnea and he made a gurgling inspiratory noise with each breath. There was no laryngeal obstruction, but the pharynx was blocked by inflamed tonsils and an abundance of mucus. The removal of the mucus gave only temporary relief from the dyspnea. Because of the marked dyspnea the adenoids were removed with Chatellier adenoid forceps; no anesthesia was given. After a little oozing there was a discharge of mucus through the nostrils, and the pharynx was free so that nasal breathing was reestablished. On the third postoperative day, the temperature returned to normal. This procedure is employed for infants with adenoids which prevent proper breathing, especially when they are taking their feedings either at the breast or from the bottle. The youngest infant who underwent this operation was 2 days old. The curet is not employed until the infant reaches the second year, when curettage is generally necessary to remove completely all obstructing adenoid vegetations from the nasopharynx.

BENJAMIN, Montreal, Canada.

A CASE OF FIBROUS SOFT PALATE IN AN INFANT. LOUIS LEROUX, Bull. Soc. de pédiat. de Paris **27**:429 (Oct.) 1929.

The infant's cry was hoarse and nasal since birth. Breast feeding was impossible as the infant could not suck properly, and at first there was some difficulty in taking the feedings from a bottle. Some of the feeding was usually regurgitated through the nose, never through the mouth. Leroux examined the infant on the fourth day after birth. The only abnormality present was in the soft palate, the middle third of which was whitish in marked contrast to the pink color of the surrounding mucous membrane; it had the appearance of a wide, vertical, fibrous band extending from the border of the hard palate to the uvula where it spread out but did not penetrate the uvula, and it did not quite reach the free edge of the soft palate. The infant did not regurgitate the food through the nose after the age of 3 weeks. At the age of 4 months the infant's development and weight were normal; the hoarse cry was still present, and the sensation and motility of the soft palate were diminished to about the same extent as they were when the child was first examined. After a number of years, the fibrous zone will probably have the appearance of an abnormally wide raphe.

BENJAMIN, Montreal, Canada.

MODERN ASPECT OF ANATOMY OF TONSILS IN RELATION TO GERMINAL CENTERS AND LYMPHOCYTES. K. A. HEIBERG, Folia oto-laryng. **19**:209 (March) 1930.

The surface of the tonsils is not indicative of their pathologic condition according to Heiberg. It is only by microscopic examination of the adenoid tissue that the severity of infection of the organism may be inferred and a guide in prognosis found. The centers of phagocytic activities (or germinal centers) especially show variations of structure which have been found to correspond to the degree of involvement. They are larger in the healthy organism, pointing to a metabolic relation. The author refers to his previous papers on this subject. On the basis of a study of 100 cases obtained from operations performed at the Finsen Institute, Heiberg does not find any difference in the behavior of pharyngeal and palatine tonsils. The activity of the germinal centers, according to Heiberg, appears to lie in the direction of destruction of lymphocytes, whereas production of the latter takes place in other parts of the tissue. The lymphocyte cap surmounting the germinal centers is larger if these are defective, and several distinct types may be distinguished in their organization. The structure of the lymphocytic nuclei is more highly differentiated in the adenoid tissue than in the lymphocytes of the blood or in those seen in infiltrations surrounding the blood vessels in acute inflammations. Greater development of the interstitial tissue is found in infections. However the rôle of immunity and metabolism is not clearly defined as yet. Heiberg points to the substance which was isolated by von Schmidt in 1927 from the germinal centers of the tonsils. It was found to be thermostabile in acids after removal of the proteins, and it caused lymphopenia after subcutaneous injection. Stimulation of the tonsils by "massage" has likewise caused lymphopenia.

[ARCH. OTOLARYNG.]

THE CHARACTER OF THE MIDDLE EAR INFECTIONS OF THE 1926-1927 LA GRIPPE EPIDEMIC. L. POLEĎNÁK, Časop. lék. česk. **67**:359 (March 2) 1928.

A comparison of the epidemics of 1926-1927, 1889-1890 and 1918-1919 is made. It was found that in 1889-1890 there was a great deal of otitis media with involvement of the nerve mechanism and impairment of hearing. In 1918-1919, there was a preponderance of the hemolytic type of pneumonia. In 1926-1927, the infections of the middle ear were of a very mild type.

STULIK, Chicago.

Diseases of the Skin

RADIUM TREATMENT OF CAVERNOUS HEMANGIOMA AND OF EPULIS. A. STRAUSS, Am. J. Roentgenol. **19**:265 (March) 1928.

The author reports the results obtained on twenty-two children, nineteen of whom were under the age of 1 year, who were treated for cavernous hemangioma by using 12.5 mg. radium needles on the skin or 0.5 mm. silver capsule radium, but 1 cm. from the skin, at from four to eight week intervals. The author states: (1) healing took place without telangiectasis; (2) treatment is simple; (3) no other agent is necessary; (4) it is applicable in infants with better results than in adults; (5) soft gamma and some beta irradiation is compatible with a good result; (6) ulcerated hemangioma responded quickly to treatment.

Epulis, a periosteal giant cell sarcoma of the alveolar border of the jaw which is of low virulence, tends to recur and does not tend to metastasize. Histologically, it is of the osteoclast type of giant cell in a fibrillar network, usually of spindle cells. These patients were treated by inserting 5 mg. needles, with good end-results.

STULIK, Chicago.

ACRODERMATITIS CHRONICA ATROPHICANS TREATED BY SYMPATHECTOMY. R. LERICHE and R. FONTAINE, Bull. Soc. franç. de dermat. et syph. **36**:803 (July) 1929.

The patient was 12 years of age and presented typical acrodermatitis chronica atrophicans of the right leg of two and a half years' duration. A perifemoral sympathectomy was performed in June, 1925, by Leriche. From that time the process appeared to be arrested, and there was great improvement in gait. The skin was more supple. In March, 1927, a right lumbar ramisection was performed. Since then there had been progressive improvement.

[ARCH. DERMAT. & SYPH.]

PSEUDOSCLERODERMAS OF INFANTS. DISS and WORINGER, Bull. Soc. franç. de dermat. et syph. **36**:960 (July) 1929.

Diss and Woringer divide these disorders into three groups: (1) lipophagic granuloma, (2) sclerema and (3) true scleroderma. The first type is most common. It has been given a variety of names (subcutaneous adiponecrosis, Fettsclerose, etc.). Lipophagic granuloma is due to a change in the subcutaneous fat following obstetrical trauma. The indurations begin a few days after birth and disappear within three or four months. Histologically, the process is confined to the subcutaneous tissues. Anatomically, there is a decomposition of fats into fatty acids and these, acting as foreign bodies, provoke a foreign body reaction.

There is no accord concerning sclerema. Classic opinion admits an adipose and an edematous sclerema. Sclerema is a symptom of debility in the new-born infant and appears commonly in premature infants who have definite hypothermia. It is fatal. The solidification of fats seems based on three factors: a special chemical constitution of the fats, hypothermia and dehydration. Scleredema is very rare, and the prognosis is not so grave as in the foregoing type. Its pathogenesis is not well understood.

True scleroderma occurs in infants, but very rarely. Most of the reported cases should be classed as lipohagic granuloma.

[ARCH. DERMAT. & SYPH.]

FOUR CASES OF FAMILIAL XANTHOMA. HUFSCHMITT, Bull. Soc. franç. de dermat. et syph. **36**:1109 (Dec.) 1929.

In this family, four of five children were affected. The disease appeared between the third and fourth year. Each of the children had articular rheumatism about the tenth year. Examination of the blood in two patients showed hypercholesterolemia, hyperuricacidemia and hypoglycemia.

[ARCH. DERMAT. & SYPH.]

THE TREATMENT OF TINEA CAPITIS WITH THALLIUM ACETATE. M. FABRE, Bull. Soc. franç. de dermat. et syph. **36**:1177 (Dec.) 1929.

The author reports the cases of sixteen patients who were treated by this method with satisfactory results. He found that a dose of 7 mg. per kilogram of body weight was sufficient. None of the patients had any noteworthy ill effects from the drug.

MICHAEL, Houston, Tex.

A CASE OF ACRODYNIA IN A BREAST-FED INFANT NINE MONTHS OF AGE. H. JANET and B. WICHSLER, Bull. Soc. de pédiat. de Paris **27**:443 (Oct.) 1929.

A girl, aged 9 months, was breast fed and perfectly healthy. A marked change in disposition, anorexia, insomnia, photophobia, marked sweating, some swelling of the palms and soles with marked redness and itchiness and later desquamation of the skin began to develop in these areas. She had a fairly typical case of acrodynia. She was given ultraviolet exposures and 5 cg. of suprarenal extract

daily and continued to be breast fed. She showed gradual improvement. The pathogenesis of acrodynia is as yet obscure. The authors do not subscribe to the theories that an alimentary toxin is the causative factor or that it is a deficiency disease; they lean more toward the hypothesis that an infectious virus, somewhat akin to that of encephalitis, is the etiologic factor.

BENJAMIN, Montreal, Canada.

PRIMARY ASPERGILLUS INFECTION OF THE SKIN AS A COMPLICATION OF MICROSPORON IN A CHILD. C. L. KARRENBERG, Dermat. Wchnschr. **88**:89 (Jan. 19); 125 (Jan. 26) 1929.

Nine days after roentgen epilation of the scalp for a patch of *Microsporon (Audouini)*, a child, aged 6 years, developed a grayish-yellow, elevated, vesiculopustular eruption on the neck which rested on a well marked, inflammatory base. No general symptoms existed. The clinical appearance of this lesion did not appear to be caused by *Microsporon*, and cultures and microscopic examination revealed *Aspergillus flavus* but not *Microsporon*. *Aspergillus* was recovered at different times from several regions on the neck. However, this parasite could not be demonstrated in histologic sections of the lesions. The author inoculated the cultures into his arm in two places and produced a lesion similar to but less intensive than that on the patient. Retrocultures of *Aspergillus* were obtained from the lesions produced on the author. The question arises whether or not *Aspergillus* was the cause of the eruption on the neck. There is a good discussion of the immunology of *Aspergillus*.

McCARTHY, Washington, D. C.

DERMATITIS EXFOLIATIVA IN YOUNG CHILDREN. O. BÄUMLER, Jahrb. f. Kinderh. **123**:170 (March) 1929.

Bäumler observed in two boys, from 3 to 4 years of age, a condition that seemed to be etiologically and pathogenetically the same as Ritter's dermatitis exfoliativa neonatorum. The disease began with angina and in one case was ushered in by severe general symptoms. Hemolytic staphylococci were found in the vesicles.

A. B. ABT, Chicago.

SPOTS ON THE KNEES AND OTHER REMAINS OF VERNIX CASEOSA. E. MAYERHOFER, Ztschr. f. Kinderh. **48**:282, 1929.

In excessive formation of vernix caseosa, remains of it may last until the sixteenth week, resisting the usual baths with soap and water. The causes are exogenous and endogenous. The cause outside of the child lies in the hormones of the mother, that is, in the so-called pregnancy toxins of Halban, which cause the formation of sebum in the child in utero and after birth. The cause within the child is constitutional—a special tendency to respond excessively to the stimulation of exogenous hormones. Especially marked as a part of the picture were the symmetrical spots on the knees, hitherto not described in infants. Outside of theoretical interest, there is a practical side, in that these children are sometimes thought not to be properly bathed. All persistent signs of vernix caseosa can be quickly and easily removed by fat dissolving agents, especially benzine.

EMERSON, Boston.

Surgery and Orthopedics

ABSCESS OF THE LUNG: A BACTERIOLOGIC STUDY BASED ON ONE HUNDRED AND EIGHTEEN CASES. CARL J. BUCHER, Am. J. M. Sc. **179**:406 (March) 1930.

The author presents a bacteriologic study based on 118 cases; he gives details of the methods and a chart of predominating organisms found in abscess of the

lung aspirated bronchoscopically. Streptococci were found most commonly in these cultures. The author's conclusions are that the organisms found in pulmonary abscesses are similar in the most part to those found in the mouth and upper respiratory tract, and that many of the organisms found in the abscess cavity gained entrance from the mouth and upper respiratory tract, through the air passages.

HENSKE, Omaha.

FORTY-TWO CASES OF APPENDICITIS IN CHILDREN OCCURRING DURING AN EPIDEMIC OF UPPER RESPIRATORY TRACT INFECTION. H. J. FREEDMAN, Arch. Pediat. **46**:604 (Oct.) 1929.

The cases were divided into two groups, those without and those with perforation. The ages ranged from 2 to 14 years. The average age of those showing a ruptured appendix was 3.3 years, which was less than the average of the other group. There was no mortality in the nonperforated group, while two patients in the perforated group died. The temperature ranged from 98.6 to 103 F. (rectal); 41 per cent of the nonperforated group had no rise in temperature, while all the cases of the perforated group had some rise. In individual cases the temperature is of little decisive value. The pulse rate was increased in both groups but very high in the cases with perforation; the variation was from 78 to 172. Thirty-six and two-tenths per cent of the unperforated group, or 19 per cent of the series, showed a pulse of less than 100. The leukocyte count was moderately elevated (12,800) in the nonperforated group and decidedly increased (16,100) in the perforated group, the general average being 14,200. In individual cases the variation was from 3,000 to 28,000. Fifty per cent of group 1, 11.1 per cent of group 2 and 33.3 per cent of the entire series showed normal or subnormal counts. The authors believe the white blood count does not contribute to the accuracy of the differential diagnosis. Possibly leukopenia in the presence of a pathologic condition of the appendix is indicative of marked toxicity.

Pyuria was present in only one case. There was no history of previous attacks in 54.7 per cent of the cases; 16.6 per cent of the patients gave a story of one previous attack, and 79.4 per cent reported pain as the first symptom. In many cases the pain was generalized through the abdomen. In 67.7 per cent there was constipation. There was practically no diarrhea. There was a history of vomiting in 85.7 per cent. In 45.5 per cent there was enough infection of the upper respiratory tract to warrant a diagnosis of acute follicular tonsillitis or acute pharyngitis.

The authors believe that many cases of acute appendicitis occur as a consequence of infection of the upper respiratory tract. Abdominal pain occurs so commonly in infection of the upper respiratory tract that pediatricians hesitate to advise operation. Emphasis is placed on physical observations, especially localized abdominal tenderness, spasm or rigidity.

The authors conclude that appendicitis may occur as a sequence of infection of the upper tract, and that perforation is more common in the earlier years.

WILSON, Norfolk, Va.

OSTEOMYELITIS: DIAGNOSIS AND NEWER METHODS OF TREATMENT. D. T. BABCOCK, J. Florida M. A. **16**:308 (Jan.) 1930.

The author emphasizes the prevalence of osteomyelitis in boys, 50 per cent of cases occurring in those between 13 and 17 years of age. The diaphysis near the epiphyseal line is the site of election. The bone-marrow is the primary focus, the process extending through the haversian canals to form subperiosteal abscesses. Early drainage through multiple drill holes may abort the infection and prevent extensive necrosis. Curetting is to be avoided.

BIEKER, St. Petersburg, Fla.

APPENDICITIS IN CHILDREN. JESSE R. GERSTLEY, M. Clin. North America **13**: 1175 (March) 1930.

Appendicitis in childhood is characterized by an insidious onset, variable and often obscure and misleading symptoms and a rapid course, frequently culminating in gangrene, perforation and peritonitis. The orderly sequence of events described by Murphy is not the rule in childhood, although the symptoms of pain, nausea and vomiting, rigidity and tenderness, fever and leukocytosis are almost invariably present. Pain is the cardinal symptom, and is constant, with no periods of relaxation. The child prefers to lie quietly, resists change of position, and will not voluntarily sit up. Vomiting is a rather constant phenomena, but is not persistent. The temperature, although elevated, usually remains at a low level, and may drop to normal following perforation. The pulse rate is increased in all cases, especially in toxic ones. Leukocytosis antedates the rise in temperature, but is never an index of the severity of the infection. Involuntary muscular rigidity is present in fully 95 per cent of cases. Palpation should be lightly done when rigidity and not tenderness is sought. The tension of the two recti muscles should be compared with one another. The muscles external to the recti are softer and should be compared with one another and not with the recti.

Skill and patience are necessary in eliciting local tenderness, as a child will usually complain of any manipulation of the abdomen. Gerstley's procedure is to gain the child's confidence by examining the right ankle, then to grasp the ankle and shake the body sufficiently to jar the abdomen. When tenderness is present, the child will often place the hand over the sore spot to steady it.

Few mistakes that a physician is likely to make have such serious consequences as the failure to recognize a ruptured appendix. No complication in medicine is more misleading. The sudden relief of all symptoms for a short time often proves to be the anticlimax of fatal peritonitis. Only by the most careful taking of the history and examination may this error be avoided.

The special conditions occurring in childhood which may be confused with appendicitis are pneumonia, pyelitis, abdominal pain associated with nasopharyngitis, "navel colic," cyclic vomiting and acidosis. Considerable uncertainty exists as to the exact cause of some of these pains, but in young children with any sort of abdominal pain, appendicitis should be suspected until definitely ruled out.

SMITH, Ogden, Utah.

ISCHEMIC CONTRACTURE OF MUSCLES OF THE FOREARM (VOLKMANN'S SYNDROME): SHORTENING OF BONES OF THE FOREARM. PAUL MATHIEU, Bull. Soc. de pédiat. de Paris **27**:236 (May 21) 1929.

A boy, aged 14 years, had suffered from a supracondylar fracture at the right elbow in 1922. A plaster cast was applied and kept over the region for one month. When it was removed it was noted that the fingers and the forearm were flexed and could not be extended properly, and there was apparently some anesthesia. In 1922, an operation was performed with very little success. The author saw the patient in 1928, when he presented the classic picture described by Volkmann, but there was no nerve injury. An operation was performed in which both the radius and the ulna were shortened by 1.6 cm.; and the cut ends of the bones were united by plates, which were removed a few months later. The patient was markedly improved so that he could write well. This form of operation is considered much better than the tendon-lengthening operations, and it should not be attempted before the involvement of the nerve, if any is present, has been treated adequately. The patient must also have sufficient intelligence to cooperate actively in effecting a return to normal in the movements of the hand and arm.

BENJAMIN, Montreal, Canada.

DISLOCATION OF THE HIP OF OSTEOMYELITIC ORIGIN REDUCED BY SIMPLE CONTINUED EXTENSION. M. FEVRE, Bull. Soc. de pédiat. de Paris **27**:240 (May 21) 1929.

A girl, aged 8 years, entered the hospital with osteomyelitis of the left hip. Incision and drainage were performed on a large abscess of the upper part of the left thigh without entering the hip joint. The child's general and local condition improved. A roentgenogram taken five weeks later, after the left lower extremity had been kept continually in extension, showed a dislocation of the hip. Because the child was running a high fever no manipulation was done, but the lower extremity was again placed in extension and abduction and the weight pulling on it was gradually increased to the maximum that the patient could bear. Another roentgenogram taken less than a month and a half later showed reduction of the dislocation. The patient was followed-up for some time, and when observed six months from the onset of the disease her general condition was good. Her temperature had been normal for several months. The bone showed good healing, she could walk with only a slight limp due to atrophy of the muscles and there was slight limitation of movement of the muscles. Locally, there was still a fistula which drained a small amount of pus. The author looks forward to continued improvement in this case. He believes that this method of reduction of a dislocation of the hip due to osteomyelitis is to be preferred to manipulation during the febrile stage.

BENJAMIN, Montreal, Canada.

A NEW METHOD OF SURGICAL TREATMENT FOR PYLOROSPASM (PYLORIC STENOSIS). KARL ZOELLNER, Deutsche med. Wchnschr. **56**:95 (Jan. 17) 1930.

To the diagnosis of pylorospasm and hypertrophy of the pylorus the author adds a third observation which he claims requires surgical intervention more frequently than the first two, that is, pyloroduodenal edema. Spasm or hypertrophy of the pylorus produces increased peristalsis with resultant hypertrophy of the gastric musculature. When the general health of the patient is reduced, the hypertrophied muscle atrophies; this in turn leads to distention, which may become very great. Because of this atrophic distention, the peristalsis is reduced, and food remains in the stomach for a long time with resultant irritating fermentation. This may produce a venous stasis and edema affecting not only the gastric mucosa but also the immediate surrounding tissue and especially the duodenum with further obstruction of the passage. The entire process, according to the author, is a true vicious circle.

In a case of this type the Ramsted operation was thought to be unsatisfactory, and the author devised the method of treatment reported. The modificaion consists of four longitudinal incisions over the area of pyloric hypertrophy extending from the pyloric region down to the duodenum. The incisions penetrate the serosa and separate the muscle coat. Experimentally in animals he observed that this permitted wider opening of the lumen, was less liable to pinch the mucosa and relieved the edema more promptly. The patient operated on was able to retain nearly all food after twenty-four hours, and gained weight within a week.

SCHERER, Duluth, Minn.

THE ETIOLOGIC THERAPY OF OSTEOMYELITIS. CANON, Deutsche med. Wchnschr. **56**:227 (Feb. 7) 1930.

The author briefly reviews his work with osteomyelitis in 1895, and cites that of Ullmann at about the same time. They used the serum of convalescent patients to protect rabbits against the intravenous injection of staphylococcus culture taken from a patient with an active case of osteomyelitis. As a result of renewal of this work and more recent investigation he recommends a number of points in the treatment: 1. All patients with osteomyelitis should be treated with the

serum of convalescent patients. If this is not available the surgical procedure should be augmented by the use of an autogenous vaccine as soon as possible after the operation. 2. Every radical operation should be preceded by a course of vaccine therapy. 3. In cases of subacute osteomyelitis and periostitis excellent results may be hoped for from the use of vaccine in the expectant treatment.

SCHERER, Duluth, Minn.

TREATMENT FOR ACUTE INFLAMMATION WITH A LOW DOSAGE OF ROENTGEN RAYS. A. VIETHEN, Jahrb. f. Kinderh. **122**:284 (Jan.) 1929.

According to Viethen, in acute inflammations the administration of from 5 to 7 per cent of the skin unit dose of roentgen rays leads to rapid cure. In the stage of fresh exudative inflammation there is complete resorption. If abscess formation has set in, this is accelerated; the surgical treatment is thus ameliorated. In younger children and in those with phlegmons, one gives the smaller doses and repeats them after several days. This procedure is recommended for erysipelas, lymphadenitis, phlegmon, furuncle and mastitis. It is contraindicated when increased suppuration may be dangerous, as in appendicitis and otitis media. After the operation, areas of osteomyelitis may heal more rapidly if irradiated.

A. F. ABT, Chicago.

DILATATION OF THE PYLORUS AS AN OPERATIVE PROCEDURE IN TREATING PYLOROSPASM. C. FORAMITTI, Jahrb. f. Kinderh. **124**:127 (June) 1929.

Besides the well known Weber-Rammstedt operation, the complications of which are hemorrhage and perforation peritonitis, Foramitti describes a method of dilatation of the pylorus which he claims gives good results. He reports eighteen cases of dilatation of the pylorus after gastrotomy. The mortality in these cases is two. Death occurred in these cases not because of the operative procedure but because of complicating infection. In a third fatality hemorrhage occurred into the abdominal cavity, postoperatively.

The stomach is opened in the middle of its anterior surface, a vertical incision 1 cm. long being made three fingerbreadths above the pylorus. A slightly curved clamp is introduced into the pylorus. The pylorus is stretched by the spreading of the clamp, following which Hegar dilators up to no. 14 are introduced. The gastrotomy wound is closed, using catgut for the mucous and muscular layer and fine silk for the serosa. A disadvantage of this method is the tearing of the serosa over the stretched pylorus. Such tears were repaired with fine silk without narrowing the stretched pyloric opening.

A. F. ABT, Chicago.

THE TREATMENT OF EMPYEMA OF THE LUNG IN CHILDREN IN THE FIRST YEAR OF LIFE AND THE TROCHAR SIPHON DRAINAGE OF PROFESSOR DRACHTER. A. HAAS, Ztschr. f. Kinderh. **48**:15, 1929.

Empyema in children under 2 years of age is caused by lobular pneumonia in the great majority of cases. This is the reason for its frequent occurrence and its high mortality, which is increased by surgical open methods of treatment, especially rib resection. Trochar siphon drainage is especially suitable for these cases.

EMERSON, Boston.

Miscellaneous

PREVENTIVE PEDIATRICS. C. H. FARMER, J. Florida M. A. **16**:404 (March) 1930.

The author makes a plea for more careful prenatal supervision, breast feeding, sunlight and regular routine.

BIEKER, St. Petersburg, Fla.

SOME NOTES ON THE ATTITUDE OF CHILDREN TO DRESS. EVE MACAULAY, Brit. J. M. Psychol. **9**:150 (Aug. 7) 1929.

This report embodies the result of an inquiry undertaken in connection with Flugel's study on the "Psychology of Dress." Three simple subjects for short essays were presented to 122 girls and 183 boys between the ages of 6 and 15 years, with the object of trying to elicit answers from which the general attitude of the children to clothing could be discerned. The questions were: 1. What sort of clothes do you like best to wear at a party? Say why you like them. 2. What sort of clothes do you like best to wear for every day? Say why you like them. 3. Are there any clothes that you dislike, and would do without if you could? Say why you dislike them.

From a study of these essays the author concludes as follows: (1) Children, up to about the age of 9, look on clothing simply as being decorative and would probably, if free to choose, wear anything so long as the color is sufficiently brilliant. Clothing has little if any significance for the self, and is not considered when the claims of the body for physical enjoyment are to the fore. From the tenth to the twelfth year the desire for decoration increases, and some very slight attention is given to the actual design and cut as well as to color. The edicts of convention also oppress the child during this period, and there is some conflict between the desire of the body for unrestricted enjoyment and the necessity of caring for and considering the clothes. During adolescence begins the sublimation of interest from the body on to the clothes, probably accompanied, on the part of the girls, with a certain amount of consciousness of sex. (2) The motive of modesty is strongly considered in connection with clothes so far as the females in the lower sections of society are concerned. Those at the bottom of the social scale have been unwilling to accept the now widely held opinion that a lightly veiled body is not necessarily and deliberately immodest. (3) Children are particularly intolerant of tight or rough garments, and quickly find their clothing too hot. Probably the unconscious impulse, up to the ninth or tenth year, is in favor of nakedness.

PEARSON, Philadelphia.

THE CHILD IN MORAL DANGER AND THE JUVENILE COURTS IN BELGIUM. I. MAUS, Rev. internat. de l'enf. **9**:99 (Feb.) 1930.

The question of the child who is in moral danger is broader than the one ordinarily dealt with by the juvenile court, as it concerns a great number of children who would not ordinarily come under a court's jurisdiction. The problem has three aspects: (1) before, (2) in relation to and (3) after the action of the juvenile court.

1. Here, as elsewhere, prevention is vastly more important than cure. In order to effect this, the causes of moral danger must be ascertained. Belgium has two medicopedagogical institutions, one for boys at Moll and one for girls at St. Servais-lez-Namur. In these schools all the factors that have contributed and determined the misconduct of the children are studied. The chief source of danger to the child's morals in Belgium appears to be unwholesome family environment; this is the case in 79.8 per cent of the boys and in 74.6 per cent of the girls. The confusion and lack of training incident to an unsettled family life contribute more than anything else to the moral disintegration of the children. To cope with this situation there has been organized in Belgium an international commission of education which, through its conferences, seeks to attack the evil at its root. When the social status of the father and mother does not meet with the approval of the commission, supervision of the children rests with the family council or with the tribunal, the expense incident to this method of control is borne by the state unless the children have property interests which may be attached. A further cause of moral danger to the young is the moving picture theater, although the law forbids admission to children under 16 years except when educational films are shown; figures prove that the cinema has been a cause of

delinquency in 39 per cent of the boys and in 77 per cent of the girls in the schools named. The author suggests that the age for admission be extended to 18. Dancing halls, pornographic literature and objectionable pictures are also among the factors constituting a menace to healthy moral life. The slums, with their wretched lodging houses where adults and children are crowded together without regard to sex, are also a demoralizing influence. A further recommendation is made to extend the age of compulsory education to 18 years; at present it is 14 years. Special schools or classes for the mentally and physically abnormal — crippled, deaf, dumb and epileptic — are suggested. In 31 per cent of the boys and in 61 per cent of the girls, alcoholism in the parents is a source of a broken family tie. The government and many private temperance associations are making a strenuous fight against this evil, so that the consumption of alcohol has diminished 50 per cent since 1913.

The curve of delinquency conforms absolutely with the curve of economic depression. Employment and the social status of the working class has diminished the number of convicts and inmates of almshouses.

2. Legislation in Belgium is remarkable for its distinctive social character. In every district special tribunals deal with children who have committed offenses or who are in moral danger from their surroundings. The presiding judge may utilize all measures necessary to protect and educate the children submitted to his care and may, if he considers it proper, remove a child from its home and assign it to some one of the societies carried on for that purpose by either public or private funds. Punishment is replaced by training and educational methods, and the personality of the child is carefully studied. Probationary terms may be given so that the reaction of the child to discipline and study may be observed.

3. When a case is completed, the judge places the child under the surveillance either of its own family or of some delegate in the association for the protection of the young. The child remains under the supervision of the judge until the age of 21.

AMESSE, Denver.

THE JUVENILE COURT: IS IT A SOLUTION? A. AICHHORN, Rev. internat. de l'enf. **9**:195 (March) 1930.

Youth in moral danger was given little or no consideration in the past; criminals, young and old, faced the same punishment for offenses, and society cared little what happened to them afterward. All of the more advanced countries now have special codes for juvenile offenders. These countries recognize that punishment of itself is not the solution of the problem of delinquency, and all admit that education of the proper sort may be infinitely more efficacious, but, in the actual administration of these laws, no fundamental change is shown in the public attitude toward wayward boys and girls who come in collision with the statutes.

The author makes a plea for guardianship education in which the juvenile court should play a part, but not in the sense of a final arbiter. "Nobody can forbid society to protect itself against the young offender, but the latter cannot in turn be forbidden to make society responsible for his neglected condition."

AMESSE, Denver.

THE CARE OF MORALLY ABANDONED CHILDREN IN POLAND. M. GRZEGORZEWSKA, Rev. internat. de l'enf. **9**:212 (March) 1930.

The author discusses measures now in operation throughout Poland to save children who by reason of their environment will eventually become public charges. Juvenile courts are being established in the larger cities to deal with all patients under the age of 17; children are removed from homes in which criminals congregate and are turned over to the state for their education and guidance. Child welfare delegates are appointed by the judges to supervise those in moral danger through neglect, unsuitable occupation and faulty training. Special schools have been opened at Warsaw, Lodz, Vilna and Herby for the prevention of delinquency;

these institutions are conducted on the group or family system. Cooperating with these are many private organizations and the National Boy Scout Society. A training institute for teachers was founded in 1921, and the efficiency of the special schools has been notably increased since that period.

AMESSE, Denver.

RACIAL PREJUDICES OF CHILDREN OF SCHOOL AGE. G. H. GREEN, Rev. internat. de l'enf. **9**:233 (March) 1930.

Following a suggestion made to the educational advisory board of the Welsh branch of the League of Nations Union that efforts should be made to counteract the racial prejudice fostered among Welsh children by the cinematograph, a serious inquiry has been instituted, in the form of a questionnaire conducted by officials of the University College at Aberystwyth.

It was first deemed essential to overcome certain objections, such as: (*a*) It should not be assumed without actual evidence that the moving picture fosters race prejudice. (*b*) There is no conclusive proof that racial antagonism exists among children, few of them having met any considerable number of foreigners. (*c*) If such antipathy exists, it is probably due to more than one agency, and all of these agencies should be determined before their relative importance is estimated.

With these criticisms in mind, two questionnaires were submitted, bearing on possible racial hatred among the public school children of Wales. The results of this investigation showed that with only a few exceptions there was a pronounced preference for certain peoples and a corresponding freely expressed aversion for others. It was found that their opinions could be ascribed to the influence of schools, newspapers, the home, personal experience and cinemas, 10 per cent to each, and 50 per cent to books.

AMESSE, Denver.

INFANTICIDE BY CUTTING THE THROAT. D. PEROTTI, Riforma med. **45**:648, 1929.

Three large, deep cuts were found on the throat, shoulders and abdomen of a new-born infant. Many superficial cuts were scattered all over the body and involved only the upper layers of the skin. The wounds appeared anemic. The umbilical cord was not ligated. The cadaver was otherwise clean. All the internal organs showed pronounced anemia. The floating test of the lungs proved that the infant had breathed. It was assumed that the severe anemia was the result of the umbilical hemorrhage, and at first it could not be positively stated if the many wounds were inflicted during life or after death. In the latter instance there was the possibility of an attempt to dismember the body. It was considered that histologic examination of the lungs would solve the problem. As the wound of the throat had severed the large blood vessels of the neck and the trachea and esophagus, the blood would have reached the bronchi and been aspirated into the pulmonary alveoli if the child had been alive and breathing. If, however, the throat had been cut post mortem, the blood would not have penetrated beyond the bronchioles, owing to the absence of respiratory movements. Microscopic examination of the lungs disclosed that the alveoli were filled with blood; this proved that the deep cut through the entire neck and throat was inflicted during life. The multiplicity of the cut wounds, their irregular distribution and their apparent superfluous nature led one to assume that the mother was in a perturbed state of mind.

MILOSLAVICH, Milwaukee.

THE FOURTEENTH ANNUAL FESTIVAL OF INFANCY. Med. de los niños **30**:293 (Oct.) 1929.

For the past fourteen years this feast has been celebrated under the patronage of the Instituto Nipiologico Martinez Vargas, devoted to the study of infant mortality. Through the efforts of the institute a great reduction in infant mortality has been effected. From 1906 to 1925, 339,092 stillbirths occurred in Spain,

an average of 17,000 a year. A study of the infant death rate shows that 2,000,000 died during the first year of life and an additional 1,500,000 before the age of 5.

In 1900, the death rate was 28.9 per thousand inhabitants, but in 1928 the rate was 19.7. In the five year period between 1921 and 1925, the death rate in Spain, compared with that of other countries, shows: Spain 20.4, France 17.4, Germany 13.5, Belgium 13.4, Switzerland 12.4, England 12.3 and Sweden 12.

DWYER, Kansas City, Mo.

EXERCISE AND GYMNASTICS OF THE INFANT. J. SCHOEDEL, Jahrb. f. Kinderh. **123**:316 (April) 1929.

When the mother's entire time is devoted to the care of the infant, sufficient bodily exercise is provided by the usual home care, play and manipulation of the limbs. In institutions, in which this is not possible, Schoedel recommends systematic gymnastics according to the plan of Newmann-Weurode, which must be carried out under the care of a physician. This is a means of combating hospitalism.

A. F. ABT, Chicago.

THE CHANGING OF THE TEETH AS AN INDICATION OF THE CHILD'S DEVELOPMENT. M. JONOFF, Jahrb. f. Kinderh. **123**:336 (April) 1929.

The changing of the teeth is to a certain extent a good index as to the physical and intellectual maturity of the child. Jonoff notes that children with delayed changing of teeth are usually backward physically, possess a bad heredity and live under unfavorable social conditions.

A. F. ABT, Chicago.

INJURIOUS EFFECT OF NAUTISAN RECTALLY ADMINISTERED. FELIX WEISS, Monatschr. f. Kinderh. **46**:419 (March) 1930.

Nautisan is apparently a proprietary remedy with chloretone as the main ingredient. It is used for the vomiting of infants. It is generally considered harmless. In an infant, aged 7 months, the use of the drug was followed by collapse. The child was entirely apathetic, and acted in every way as if under anesthesia. Following cessation of the administration of the drug there was speedy recovery.

GERSTLEY, Chicago.

ACETYLSALICYLIC POISONING. H. KRASSO, Wien. klin. Wchnschr. **42**:1594 (Dec. 12) 1929.

The author's patient took 30 Gm. of acetylsalicylic acid with suicidal intent, but recovered after severe symptoms. These were toxic rather than anaphylactic. The author gives a full review of the literature.

CLAUSEN, Rochester, N. Y.

LEONARD BOURDON'S SYSTEM OF INSTITUTIONAL DISCIPLINE (1788-1795). S. BERNFELD, Ztschr. f. Kinderforsch. **36**:153 (Jan. 18) 1930.

Bourdon, a Jacobin of radical inclinations, was a trained pedagogue whose conceptions of child education exercised a great influence on the thought of his time and, through Fichte, on the period of the Napoleonic wars. He regarded institutional training as the only rational form of child training and he criticized the ideal of the Rationalists, that the family was the proper guardian of the child. The remarkable feature of Bourdon's work, however, was rather his peculiar organization of such an institution. This included such "ultramodern" ideas as self-discipline by self-elected pupil committees, and restriction of the authority of the teacher and parent-teacher associations. The description of this interesting character and his model school is well presented by Bernfeld. The theme is particularly important today in the presence of the Soviet school system and the concep-

tions of many modern child psychologists. In one respect the author's opinion must be criticized: Bernfeld's assurance that Bourdon's opposition to home training is the sublimation of early unconscious "hate of the parents" may be questioned and another hypothesis may be advanced. Practically all absolutists, whether philosophers like Plato, certain of their possession of the "truth," or whether revolutionary ideologists, also certain that they possess the panacea for all ill, will inevitably wish to impress their verities on youth. The home, which is almost shiftless in its elasticity, must be a stone in their path. Hence they turn to the institution, where young minds can be stamped with their impression.

REICHLE, Cleveland.

SEXUAL DIFFERENTIATION BY BODY MEASUREMENTS AND PROPORTIONS IN CHILDREN AGED SEVEN YEARS. W. KORNFELD and M. SCHONBERGER, Ztschr. f. Kinderh. **47**:676, 1929.

Between boys and girls there was an average difference in the standing height of about 10 mm. in 285 approximately normal children. The relative stem length was greater in the boys than in the girls during the ages studied; later the girls overtook the boys. The important leg length of girls corresponded to the earlier jump in development which came first in the long bones of the lower extremity. The values for the circumference, length and width of the head were higher in boys than in girls; this difference persisted if these measurements were compared with the average standing height. In proportion to their height the boys had larger heads than the girls. The circumference of the head constantly increased with the weight of the body. Among the medium-sized children, the form of the head was broader in the boy; the narrower heads were found in the large and in the small children of both sexes. The narrower heads of the large children went with the more common leptosome habitus found in them, with the tendency to tall and thin development, while in the middle sized children, the eurysome type went with the general development in breadth. The lower average value of the length-breadth index in the small children could be traced back to certain degenerative hypoplastic types, and even to normal children characterized by small growth and narrow heads. A regular difference between boys and girls was recognizable in the average length-breadth index of the head—in the boys the narrower, and in the girls the broader form of head.

Especially important was the constant difference between boys and girls in the absolute and relative average circumference of the wrist. It was to be assumed that at 7 years of age the boy tended to show a more solid bony structure in general than the girl.

EMERSON, Boston.

THE PROBLEM OF RIGHT OR LEFT-HANDEDNESS IN THE LIGHT OF THE EPIDERMAL CONFIGURATION OF THE HUMAN PALM. J. VALŠIK, Časop. lék. česk. **67**:205 (Feb. 3) 1928.

In checking the palm imprints of right and left-handed persons, together with those of ambidextrous students, no correlation was found. In checking carefully the so-called papillary number, no relation was found between the high numbers of various authors and those of real right or left-handedness.

STULIK, Chicago.

Society Transactions

NEW YORK ACADEMY OF MEDICINE, SECTION OF PEDIATRICS

Jan. 9, 1930

F. Elmer Johnson, M.D., *Presiding*

Encephalitic Changes in So-Called Toxicosis of Infants. Dr. M. A. Goldzieher.

Autopsy observations in cases of toxicosis are usually negative. There are no changes, or very slight ones, in the gastro-intestinal tract in spite of the severe diarrhea which is prevalent in most of the cases. Changes of the other organs are negligible or incidental. In three cases recently studied histologic changes of the brain were demonstrable which seemed to shed some light on the pathogenesis and seat of the disease.

All three cases occurred in infants, the ages of whom varied from 6 weeks to 4 months. They were all artificially fed. Two of them did well until shortly before the outbreak of the disease. In one case there was some infection of the upper respiratory tract prior to the onset of toxicosis. The symptoms of toxicosis were typical in all three cases. The patients had the characteristic color, facial expression, breathing and dehydration. They had diarrhea and vomiting. They also had high fever. Convulsions were observed in one case, while no nervous or cerebral symptoms were seen in the other two cases. All three children died in a condition of extreme dehydration in spite of the abundant administration of fluids.

The anatomic examination of two cases had a negative result. In the third case multiple petechiae were present and there were small, irregular hemorrhages over the base of the brain. There was also a right otitis media and an acute catarrhal tracheitis.

Microscopic examination of all three brains showed practically identical observations. Sections made from both hemispheres, the cerebellum and the medulla oblongata showed absolutely no changes. Sections taken from the diencephalon, however, showed both diffuse and nodular cell infiltration. The diffuse infiltration was particularly conspicuous in the gray matter surrounding the third ventricle, while the nodular foci were discretely scattered all over the hypothalamus and the brain tissue around the tuber cinereum. These nodules often consisted only of a small number of cells, while others contained 50 or 100, and a few were more extensive and covered an area two or three times as large. The cells which compose these nodules are mostly of the glia cell type, while others are obviously leukocytes. The nodules have not arisen as perivascular cell aggregations, but blood vessels which occasionally are found nearby show conglomerations of polymorphonuclear leukocytes and emigration of these cells through the vessel wall. The histologic character of the diffuse infiltration is quite similar, although there is a greater variety of cell forms in these diffuse infiltrations, and in the larger nodules than in the smaller ones. The inflammatory character of the lesion is brought out also by the presence of exudation on account of which the brain tissue appears honeycombed about some of the nodular foci. Lesions of the ganglion cells in the areas involved include shrinkage, poor staining and neuronophagia. Two, three or more phagocytes have gathered around such ganglion cells.

In the case which showed the grossly visible hemorrhages of the meninges, there was also a cellular infiltration of the meninx on top of the tuber cinereum. Otherwise, the changes were identical with those in the other cases.

The changes described in these three brains are definitely inflammatory. The inflammation is of a more proliferative type, although there is ample evidence of hyperemia, exudation and emigration of leukocytes from the blood vessels. These changes are restricted to the interbrain and could not be found in any other part of the central nervous system examined.

The localization of these lesions to that part of the brain which is supposed to harbor the regulatory centers of water metabolism points to a relationship of these lesions with a disturbance of water metabolism in the clinical syndrome of toxicosis. Dehydration of such infants is apparently due to the fact that their tissues are unable to retain water. It is true that loss of water by vomiting and diarrhea is considerable, yet it is not in proportion to the extent of dehydration. In some cases vomiting and diarrhea are practically negligible and still dehydration is just as severe. It is reasonable to assume that there is a considerable loss of water through the lungs and skin. The loss of water could not be explained by the conception of toxicosis as an intestinal disease.

Schiff's experiments on dogs have shown that the clinical picture of toxicosis can be produced by restriction of the intake of water provided the animals are fed a diet rich in protein. Yet, these animals would recover from their ailment if fluids were forced, as they are on infants suffering from toxicosis. This seems to indicate an essential difference between the experimental form of toxicosis and the infantile disease.

The changes described in these three cases are not similar to those observed in epidemic encephalitis or in any other forms of encephalitis concomitant to ordinary infections. The latter are characterized by the definitely perivascular arrangements of cell infiltration.

The localization of the lesions to one particular area of the central nervous system has its analogy in the distribution of the lesions in poliomyelitis. This would suggest an infection of a specific kind.

The small number of cases presented does not warrant sweeping conclusions. It is possible that no encephalitic changes will be found in other cases of toxicosis. If so, toxicosis will have to be divided into an encephalitic and a nonencephalitic type. The lesions of the interbrain, as described, would suffice to explain both dehydration and the frequent nervous symptoms such as convulsions, drowsiness and rigidity of the neck. They are so conspicuous sometimes that such cases have been spoken of as hydrocephaloid.

Summary.—Changes in the brain in three cases of so-called alimentary toxicosis are described. The changes are of the proliferative inflammatory type. They localize in the interbrain. The presence of encephalitic changes about the centers, which are supposed to regulate water metabolism, suggests causal relationship between encephalitis and dehydration.

The term diencephalitis dehydrans is proposed in order to describe the disease which is characterized by inflammatory lesions in the interbrain and by dehydration as the outstanding clinical symptoms.

DISCUSSION

DR. HERMAN SCHWARZ: When I was asked to discuss this paper and I heard that Dr. Goldzieher had found an anatomic basis for this clinical picture, I was very much interested. If we can determine the underlying pathologic lesion, it will be a great step toward explaining many of the symptoms which we encounter.

I am going to base my discussion first, on the clinical picture, as I know it, and try to see whether I can connect therewith an anatomic basis, and secondly, I am going to tell you about five cases which we have had the opportunity of examining pathologically.

When Dr. Goldzieher's paper was shown to me I asked Dr. Globus, neuropathologist at Mount Sinai Hospital, to examine some of the brains from our cases. Therefore, I shall ask the chairman to call on Dr. Globus, who will tell of the pathologic observations, if any, in the midbrain, the floor of the fourth ventricle and the tuber cinereum of five typical cases of alimentary toxicosis. In a paper written some time ago, I eliminated the word "alimentary" from part of the name, because even to this day we are not sure of the alimentary basis of this condition.

I am not so sure that dehydration is present in all instances. I have seen cases in which loss of water by vomiting and diarrhea was negligible, and still the symptoms were present. In the winter one will occasionally see infants with bacteremia with similar symptoms. Even though no diarrhea and vomiting are present, there may still be dehydration. The work of E. Schiff has shown that dehydration alone in young infants does not always produce these symptoms. It is also shown in animals that the simple withdrawal of water does not necessarily give toxic symptoms unless protein is added. In other words, there are other things such as changes in the electrolytic milieu which bring about the toxic symptoms. As far as the water metabolism and the brain are concerned, I might say that in studying cases of nephritis I was fascinated by the connection of the midbrain with water metabolism. The interchange of fluids between the blood stream and the tissue spaces, the interchange between the cells and the tissue spaces and the blind ending of the lymphatics in the tissue spaces all make the question of water metabolism difficult. Dr. Goldzieher's connection of this whole subject with the lesion in the midbrain is what the Germans would call "a genial idea."

Dr. Joseph H. Globus: My discussion will consist of a report on a study of five cases of alimentary toxicosis. I have investigated the tuber cinereum and have failed to disclose any lesion, inflammatory or degenerate, in any of these cases.

I have checked up our material by studying three control cases of infants of a similar age. One must bear in mind that there are many pitfalls in the study of the brain of an infant, since it is not yet fully developed, and no pathologist can be entirely sure of his ground in such material. A small collection of cells, here and there, and some altered blood vessels are not necessarily of pathologic significance and, unless checked up, may erroneously be regarded as evidence of a lesion capable of producing clinical manifestations. We have found such collections of glia cells, here and there. We know that they are likely within the limits of normal.

As regards the material presented by Dr. Goldzieher, I would say that he has not been able to demonstrate an inflammatory lesion except in one case. He has not established his point. I think that he has been misled by some of the collections of cells in the subependymal zone as being abnormal, but if he had studied normal material, he would have also concluded that these were immature cells, which have not yet assumed their normal character and position.

The idea of Dr. Goldzieher, I think, is worth while following up, but one must be exceedingly careful with material obtained from immature brains, and no conclusions should be drawn unless the study is checked with normal brains of the same stage of development.

Dr. M. A. Goldzieher: I was greatly pleased to hear that five other cases of alimentary toxicosis had been examined. I agree with Dr. Globus that it is extremely difficult to judge changes in the brains of infants. I am thoroughly familiar, of course, with the fact that foci of embryonal nerve cells occur in such brains. It also stands to reason that such lesions, as I have demonstrated here, should be compared with more than two, three or even five normal brains in order to draw conclusions.

The character of immature nerve cells, of course, is altogether different from that of the cells of these lesions. The nodular character of the changes described

is definite. Although they are not perivascular, there are often small blood vessels nearby showing a collection of leukocytes and emigration into the adjacent brain tissue. When Dr. Globus stated that I proved the inflammatory nature of the lesion in only one case he seems to be mistaken. All the changes were practically identical in two of my cases and almost identical in the third. I believe in the necessity of examining a larger number of such cases in order to clear up controversial points.

I appreciate the clinical remarks of Dr. Schwarz, yet I feel that the symptom of dehydration in the toxicosis of infants is of the greatest significance. This seems to be emphasized by the name of the disease used by German authors. In the German literature it is referred to as "Exsiccosis," which means dehydration.

A Possible Explanation for Horse Serum Anaphylaxis in Man. Dr. Bret Ratner.

Experimental and clinical observations were presented which the author deemed convincing enough to offer as a possible explanation for the particular natural hypersensitiveness to horse serum encountered when a child or an adult, on receiving an injection of horse serum for the first time, dies in acute anaphylactic shock or manifests grave accelerated allergic reactions. (This work was done at the Syndenham Hospital and the Departments of Pediatrics and Immunology, University and Bellevue Hospital Medical College, New York University. The work is being carried on under the Crane Research Fund for the Study of Allergic Disease in Children.)

While the possibility of anaphylactic death following an injection of horse serum looms large in the imagination of the physician, it is in reality an exceedingly rare occurrence.

From the experimental and clinical observations, the following conclusions were reached. An anaphylactic relationship exists between horse dander and its homologous serum. This common substance is resident in the globulin fraction of the respective antigens. Guinea-pigs sensitized with horse dander can be shocked with horse serum. The reverse sequence can be accomplished but rarely, and only when large doses are used. This relationship has been demonstrated by parenteral injection and by the uterine strip method. This relationship has been further demonstrated by the inhalation method which most closely simulates the situation to which the human being is subject. Animals naturally sensitized through the inhalation of horse dander died in anaphylactic shock or showed grave anaphylactic symptoms on receiving a first intravenous injection of horse serum or diphtheria antitoxin.

Clinical cases were presented to show that anaphylactic death or accelerated anaphylactic reactions following the primary injection of horse serum or horse serum antitoxin occur in persons spontaneously hypersensitive to horse dander.

Human beings may be artificially sensitized by large injections of horse serum. Such persons are less susceptible than asthmatic patients who are spontaneously sensitized to horse serum.

It is improbable that toxin-antitoxin can artificially sensitize a person to horse serum.

Only such persons who are shown to be sensitive to both horse dander and horse serum should be considered as risks for the primary administration of horse serum. If it should be imperative to administer horse serum for therapeutic purposes, the greatest precautions should be observed to give the serum exceedingly slowly and by the route of least absorption, together with the utilization of such drugs as epinephrine and atrophine.

DISCUSSION

Dr. William H. Park: For several years, I have been greatly interested in Dr. Ratner's work and have been impressed by the care with which he has endeavored to prove everything either by experimentation on animals or by

investigation in human beings. It is important to remember that when we speak of horse dander or serum, we are not speaking of a definite chemical substance. There is always some serum in horse dander, so that when a large amount is inhaled, more or less horse serum is also inhaled, and animals may or may not become sensitized to it according to the amount received.

There is such a minute amount of horse or goat globulin in the preparation of toxin-antitoxin in general use that it does not seem probable that sensitization could be obtained by the tiny amount given in any but exceptional persons. As you know, for immunization three doses of toxin-antitoxin, each containing only 0.003 cc. of blood serum, are given. I have had a number of chances to watch a group of children, part of whom had received toxin-antitoxin and part of whom had not; all of the children later received doses of diphtheria or scarlet fever antitoxin. There was no appreciable difference in the reaction of the two groups to the serum.

Yet, we must acknowledge the possibility, though not the probability, of definite sensitizing by this minute amount of horse globulin. Hooker showed that a number of students receiving 1 cc. of 1:100 solution as a skin test and then three doses of the old preparation of toxin-antitoxin were sensitized. It must be remembered that he had to give the previous dose to find out if they were already sensitized. In other words, he gave thirty times as much serum as we now give. He discovered an increase in reactions of the skin from the combined injections, though none showed any marked reactions.

We tested the question in a different way by injecting 0.01 cc. intradermally into 100 children who had had toxin-antitoxin and into 100 who had not had toxin-antitoxin; the same procedure was followed in an equal number of adults. There was only a very slight average increase in the severity of the reactions.

One of my students at the university, Miss Behner, has carried on a large number of experiments to see whether such a tiny amount of horse serum given to guinea-pigs would create appreciable sensitization. We produced a slight sensitization in only a small percentage of guinea-pigs. Following an injection of 1 cc. of serum, intracardially, there was a little scratching and uneasiness, but nothing severe. We tried injections of tiny amounts of goat antitoxin, and the guinea-pigs that received the doses showed no crossed sensitization even when a large amount of horse serum was injected into the heart. These tests showed that there was little to fear from sensitization of human beings through the late preparations of toxin-antitoxin, but because physicians feared and because goat antitoxin is just as good as horse serum, we shifted to goat antitoxin; this has been done practically all through the United States, so that now almost no one gets toxin with horse antitoxin. As far as sensitization by toxin-antitoxin goes to later therapeutic doses of horse serum, we need not worry, or we can used toxoid, which has even greater immunizing power, but which produces more reaction in older children.

If another injection of serum is given several days after therapeutic or preventive doses of serum, much more marked reactions occur, but from intramuscular doses there is no added appreciable danger. Accidents are rare. Intravenous injections, however, occasionally give more severe immediate reactions. When second injections of serum are given from a few days to several years after the primary dose, there is usually a rise in temperature and an accelerated development of a rash. In cases of lobar pneumonia in which because of a relapse repeated injections of serum have been given from three days to a week later, there have been serious reactions but no deaths.

There have been deaths from tiny amounts of serum, even when less than a cubic centimeter of a desensitizing dose was given. When a dose of 5 cc. is given and no severe reaction occurs, the patient can receive that amount of serum later without reaction or less reaction than that which the first injection produced, but if a triple or a quadruple quantity is administered, severe reactions may occur. It is still of great importance to know the history of the case, particularly concerning the attacks of asthma. If such a history is obtained or the patient's

reaction to the eye test is marked, serum in tiny amounts is used at the start. Small amounts of serum for desensitization will show whether or not the case is one in which serum is apt to be dangerous, but it may in some instances show by killing the patient. Dr. Ratner's paper seems to be of great interest and real importance.

THE CARBOHYDRATE METABOLISM OF THE NEW-BORN INFANT. DR. HARRY M. GREENWALD and DR. SAMUEL PENNELL.

This article was published in full in the March, 1930, issue of this journal, p. 493.

URINARY CALCULI IN INFANCY AND CHILDHOOD. DR. MEREDITH F. CAMPBELL.

Urinary stones in infancy and childhood are not of as rare occurrence as is generally believed. In the presence of stone chronic pyuria is an almost constant factor. If pyuria persists for more than from four to six weeks in any juvenile patient who has been adequately treated medically, such a patient should be subjected to complete urologic examination, including cystoscopy, ureteral catheterization, renal function tests and pyelography when indicated. By this method calculi will be demonstrated. The symptoms of calculus are usually those of localized pain plus infection of the urinary tract. Symptoms of infection are most often manifested by urinary frequency, sometimes by dysuria and hematuria.

The treatment for urinary calculus in childhood is identical in all respects with that employed for this disease in adults. In many cases of stone in the renal pelvis, pyelolithotomy may be carried out, but often complete destruction of the kidney indicates nephrectomy. Ureteral stones may be passed following ureteral dilatation with bougies, but failure of the stone to pass following ureteral treatment indicates ureterotomy. Small bladder stones may be crushed by lithotripsy while large or hard stones are best removed by suprapubic cystotomy.

The mortality following these operations is low. Seventeen cases observed at autopsy and the cases of thirteen patients treated surgically were reported from the children's medical and surgical division, the departments of pathology and urology of Bellevue Hospital.

DISCUSSION

DR. A. R. STEVENS: It has always been supposed that we would find in children the counterpart of all lesions which we are accustomed to find in grownups, but until the last ten years there has been comparatively little intensive work done on this subject.

In order to realize just how important it is that we should recognize stones in young children, it is important that we should understand clearly in what way stones in the urinary tract may cause harm. They cause deterioration and gradual destruction of the corresponding kidney. They cause harm also because they encourage secondary infection, and once infection has taken hold of any part of the urinary tract, it is practically impossible to clear it up if calculus is present without having the stone removed.

Patients who are examined because of pain, hemorrhage or urinary frequency are much more apt to be considered carefully and the cause of the symptoms found, but it is persons who are comparatively comfortable or have only pyuria who are neglected and who are allowed to go from one physician to another without being carefully examined.

It is Dr. Campbell's idea, as I have gathered it, that the cases of pyuria that will not clear up on good medical care within from four to six weeks should be investigated carefully at once from the urologic point of view. We frequently come across comparatively young men with calculi and infection in both kidneys, in whom both kidneys are practically gone. It is to cut down the number of cases of this kind that we are especially keen that in the cases of pyuria that will not clear up quickly cystoscopy should be performed carefully and the patients treated properly.

March 13, 1930

F. Elmer Johnson, M.D., *Presiding*

Roentgenology of the Thymus in Infancy. Dr. Henry K. Pancoast.

Notwithstanding a wide discussion of the subject, there seem to be many conflicting views concerning the exact status of the thymic gland as a potential danger in infancy. In the midst of the many conflicting theories in regard to the cause of death in status lymphaticus and the potential dangers of an enlarged gland, as so ably summarized by Marine (1928), physicians have followed the trend of views or inclinations of most roentgenologists and pediatricians in assuming that to be on the safe side of the controversy one must regard the danger, or at least the chief one, as a mechanical problem. Dr. Pancoast believes that the study of the thymus in infancy must be approached through observations of the upper respiratory passages rather than through a study of the gland itself, as has been the common practice in the past. His conclusions have been based on a roentgenographic and fluoroscopic study of the living infant and have been confirmed by the statements of Jackson from observations made directly in the air passages during life. His beliefs do not in any way apply to the causes of death in adults supposedly from disease of the thymic glands, nor does he believe that the mechanical or obstructive factor applies in older children or adult life.

Noback and others have shown that the apex of the wedge-shaped gland in infancy may have its superior apical aspect project upward into the narrow rigid bony ring of the thoracic inlet. It is known that the gland is pushed up during expiration so that the apex of the wedge may then exert a pronounced compressing effect on the adjacent portion of the trachea. The latter structure normally collapses about 50 per cent during expiration or just as inspiration is about to begin (Jackson). This collapse is from behind where there are no cartilaginous rings. The wedge of the thymus protruding through the thoracic inlet may buckle or still further collapse the trachea against the rigid spine. Lateral compression occurs in about 25 per cent of cases (Jackson). The width of the thymus as shown by the sagittal roentgenogram, which is the evidence usually employed in interpreting enlargement, is no criterion in the exact estimation of size or potential dangers. The only signs of enlarged thymus to which any attention is paid are the following: (1) lateral deviation of the trachea as shown by the sagittal view; (2) narrowing of the trachea during the inspiratory phase at the thoracic inlet, by the lateral view; (3) too great a collapse of the trachea during the expiratory phase at the thoracic inlet by the lateral view; (4) buckling of the trachea at either phase as it passes over and behind the top of the wedge-shaped gland. This must be based on a rigid enforcement of technic, especially in regard to the position of the head.

Technic.—All patients should receive a preliminary fluoroscopic study in the sagittal and lateral directions. This must include the neck and the chest. The examiner's eyes must be well accommodated in order to see the pharynx, the larynx and the trachea. The child must be crying lustily and regularly and not sobbing. The effects of both phases of respiration should be carefully noted.

The roentgenographic exposures should be made in the erect posture in a specially devised chair and casset holder. Two exposures should be made in the sagittal direction, one during full inspiration and one during full expiration, and accurately timed. The arms should be held above the head and the head held straight, and the body should not be allowed to slump. The child must still be crying regularly. Two lateral views must be made during the two phases. The arms should be held down and behind the patient for these views. The head must be straight. All exposures must include the neck.

Differential Diagnosis.—High respiratory obstruction may be due to many other causes than enlarged thymus, and one must not be misled by the relative preponderance of the gland in infancy and overlook some other important condi-

tion. The examination must include every possible form of obstruction. Some of them cannot be found, and if the thymus does not explain the obstructive phenomena, an endoscopic examination should be advised.

The following conditions can be readily determined by roentgenologic study, and each of them has been found and has explained the symptoms in some of the cases referred for supposed enlarged thymus: foreign bodies, retropharyngeal abscess, laryngeal and tracheal stenosis, disease of the adenoids, congenital heart disease and relaxed soft tissues of the pharynx and larynx.

The stenosing effects of diphtheritic membrane and streptococcic laryngitis may be readily detected.

Certain other conditions may simulate the phenomena of enlarged thymus, and have been found to be present on further search following the elimination of the gland as the cause of symptoms. These are: asthma, whooping cough, meningitis and recurrent laryngeal paralysis (resulting from thymic enlargement).

The collapse of the soft tissues of the larynx and pharynx is readily determined. It may assist in the obstruction when the child has to pull harder to get air against the obstruction offered by the thymus. Unusual collapse of the soft tissue alone may be responsible for supposed obstructive phenomena when the thymus is not a factor.

Recurrent laryngeal paralysis may occur on either or both sides as a result of thymic enlargement. Jackson considers it fatal when it is bilateral. Persistence of obstructive phenomena after apparently satisfactory reduction in the size of the gland demands endoscopy in order to determine whether or not this complication exists.

DISCUSSION

Dr. Webster W. Belden: As usual when Dr. Pancoast presents a paper, he so clearly covers the subject that but little is left for us to discuss. The only thing that Dr. Pancoast seemed not to have stressed strongly enough was the question of the technic, which is of paramount importance.

Dr. Remer and I presented a paper some years ago, in which we insisted on the erect posture in the examination of the thymus in children. This was met with considerable opposition, and listed among our opponents was Dr. Pancoast. Since that time he and Dr. Pendergrass have been working with this method, and, as you heard, he feels that the erect posture is the proper position for such an examination.

I was rather surprised to hear him say that he did not pay much attention to the size of the thymus as seen in the films in the sagittal plane. We do feel that this widening of the shadow of the superior mediastinum in the sagittal or the anteroposterior position is of importance, and we have taken as our standard the angle of Louis. Unfortunately, this adds another man's name to medical phraseology, which is to be deplored. This angle is measured from the angle on the inner side of the third rib on both sides. If the shadow of the thymus in the sagittal plane measures one third or less the total transverse diameter of the thorax at the level of the angle of the third rib, we consider this to be a normal thymic shadow.

We are frequently confronted with the problem of the child without symptoms presenting a shadow considerably larger than one-third the diameter of the thorax, and the question arises, should this child be treated or not? We feel that treatment should be administered. On the other hand, we also have children referred to us with no evidence of thymic enlargement in either the sagittal or the lateral plane, who have symptoms. We again feel that these children should be given a course of roentgen therapy.

The question arises: Would either of these children have died as the result of trivial infection or anesthesia had treatment not been administered? This is impossible to answer.

The symptoms in thymic enlargement are legion. A few months ago a child was brought to our laboratory whose only symptom was swelling in the arms, forearms and dorsa of the hands, which appeared in the afternoons. The child was 7

months old, was normal in all other respects and was gaining weight regularly. When roentgenograms of the chest were made, we found a very large thymus in both the sagittal and the lateral plane. The child was given four treatments, and the swelling of the arms and hands disappeared. This merely illustrates the peculiar bizarre symptoms which occur as the result of thymic hyperplasia.

There are two types of thymus of children with thymic hyperplasia. One type is the fat child with pink cheeks, whose grandmother and aunts think it a wonderful specimen. The infant with this type is often found dead in bed by the mother. Death is not due to smothering by a blanket, but to enlargement of the thymus. Then there is the puny child, who has the sniffles. I have had such an experience in my own family. One sister-in-law had a small, puny child, whom she found dead; the other example was a large, fat child in the family of a cousin. Autopsies proved the existence of a large thymus in both cases. One must constantly bear in mind that even though not common, lymphosarcoma may occur.

I do not think that a differential diagnosis can be made positively in all cases. One case in my experience was in a child, aged 5. She had never been well and had had asthma since the age of 3. Roentgenograms were made and an erroneous diagnosis of enlarged thymus was offered. The child was treated both by myself and by a prominent roentgenologist in New York, and after each treatment alarming symptoms developed, and she seemed to be choking to death. The roentgenologist gave her much larger doses than I did, and the symptoms were proportionately worse. She died later, and autopsy disclosed lymphosarcoma in the mediastinum.

As to technic, the position of the head is of extreme importance. One must be sure that it is straight in the sagittal plane and that it is not flexed in the lateral plane, as a slight change in the position of the head changes the position of the trachea quite markedly in children.

One might think that it is difficult to secure expiration and inspiration films in children, but it is not. Slapping of a child to make it cry is not advisable, as the parents would consider it brutal. If one snaps the bottom of the child's foot, this is usually sufficient to cause crying. When the child is yelling at the top of its voice, he is expiring and a film snapped at this moment, with the shortest possible exposure, produces a film on expiration. When the yelling ceases, the child will gasp, and at this point he is inspiring, at which time another film should be made. I do not think that the technic of the erect posture can be overstressed.

Within a few months I have had two patients brought to me, one an infant of 9 months and the other a child of 3 years. In both cases the mothers were rich, influential women, who had been perturbed on hearing of enlarged thymus and sudden death. Both children had been said to have enlarged thymus glands. As soon as I looked at the roentgenograms I could see that they had been made with the child in the prone or supine positions. I told the mothers that I did not think that the children had enlarged thymus glands, that the children did not need treatment and that I wished to examine them again. When I examined the child, aged 3 years, in the sitting posture, the mother remarked that that was not the way it was done before, as the child was lying on her back. I then made a lateral roentgenogram and had the mother wait while the films were developed. I showed her that the child did not have an enlarged thymus in either position. I then made a roentgenogram with the child in the supine position, with the film under her back, and again produced the enlarged superior mediastinal shadow.

DR. JOHN REMER: Dr. Pancoast and Dr. Belden have covered the diagnosis and roentgenographic aspect of thymic enlargement so well that there remains but little for me to say regarding this part of the subject. I should therefore like to confine myself to some of the symptoms and the treatment for enlarged thymus, and particularly call attention to the necessity of taking into consideration both the clinical and the roentgenographic observations in the selection of cases for treatment. Frequently, in a case in which there is no roentgenographic evidence of an enlarged thymus, the clinical symptoms of cyanosis, difficult deglutition,

regurgitation of food and the like will be present. The lack of roentgenographic evidence does not necessarily mean that there is not an enlarged thymus, as the enlargement may be anteroposterior and therefore would not show on the film.

While true thymic asthma is disputed by some, it seems to me that there can be no doubt of the existence of this condition, as at the hospital cases are frequently referred to us from the asthma clinic with marked symptoms of true asthmatic attacks. Rubin reported thirteen cases of enlarged thymus in which the prominent symptom was pylorospasm with vomiting more or less persistent. In these cases, the only symptoms in the chest were cyanosis and holding the breath. In all of these cases roentgenograms showed an enlarged thymus. The vomiting and pylorospasm were decidedly improved or checked by roentgen treatment of the thymus, no other treatment being given.

The occurrence of an enlarged thymus is rather astounding; for example, those measuring more than 3 cm. at the angle of Louie. Hiss, in an examination of 119 cases, found 42 per cent, and other investigators give percentages varying from 33 to 66 per cent, depending on whether the children were born to young or older mothers, and on the number of pregnancies. While the thymic shadow practically disappears in most cases in the first year, it is surprising to note the number of cases in which it continues into adult life. Rowe said that in 65 per cent of cases in which operations are performed on the thyroid gland, a hypertrophied thymus is found.

The question has been raised as to whether or not treatment is advisable in cases of enlarged thymus without symptoms. I feel that the answer should be "yes," as in an emergency operation serious results might follow if a hypertrophied thymus were present. Also, treatment is advisable in cases in which there are thymic symptoms without roentgenographic evidence of hypertrophy. This brings up the thought that in all contemplated operations on children, roentgenograms should be made to rule out the possibility of enlarged thymus.

While several methods of treatment have been suggested, surgical intervention, radium, etc., it is to roentgen therapy that we must turn for a method that is easily available, practical and safe in competent hands. But great care must be exercised not to administer too large a "dose" at the first treatment, particularly in those cases in which there is marked hypertrophy of the thymus or in which the symptoms are markedly severe, as there is apt to be too rapid absorption of the gland, accompanied by an aggravation of symptoms and the possibility of a fatal outcome.

DR. HOWARD H. MASON: I must admit that after hearing this excellent paper, I am quite confused. It seems as though we must be dealing with two conditions; first, an enlarged thymus causing obstruction and second, the so-called status thymicus. I cannot believe that all cases of enlarged thymus are really cases of status thymicus. Deaths caused by status thymicus, as far as they are reported, are due to cardiac failure, not to respiratory failure. In the cases described, the trouble is respiratory obstruction. I cannot see that all deaths caused by thymic enlargement are obstructive. From the evidence it seems that a great many cases are due to cardiac and not to respiratory involvement.

The difficulty is that the two conditions cannot be correlated. What we need clinically is some way by which we can identify the disease in children, some means by which we can make the diagnosis beforehand and thus be in a position to do something. I think that we all send patients with large thymic shadows for roentgen treatment. I have tried to find a report of a case in a patient who received such treatment and who died afterward, due to the presence of an enlarged thymus, but I have not been able to find such a record. While we treat all patients, I think that a great many of us have some doubt as to just what we are accomplishing when we do this. I have wondered sometimes what would happen if we made roentgen radiation on some other part of the body.

Possibly one group of patients has a large thymus that compresses the trachea and thus may cause respiratory embarrassment at times, while the second group is composed of those cases that we now call status lymphaticus. In the latter group, the thymus is usually large but may not compress the trachea. In this group death is due to cardiac failure and is probably not due to tracheal obstruction.

DR. OSCAR M. SCHLOSS: The work reported by Dr. Pancoast seems to be of the greatest importance and offers a means for the determination of the presence of thymic obstruction and an appraisal of its extent.

There is little question that the ordinary sagittal view of the thymus gland may be misleading. At autopsy, one frequently sees glands that would cast a large shadow on an anteroposterior view and yet are not thick, while other glands that would appear small are much thicker and perhaps more likely to cause obstruction.

I have felt for some time that the size of the thymus gland is definitely related to nutrition. I have never seen a large thymus shadow in a malnourished infant, and on several occasions I have seen the shadow fluctuate in direct relationship to the child's nutrition. The same is equally true of postmortem observations.

I am glad that the speakers confine their remarks to thymic obstruction. There is a great tendency at the present time to attribute any symptom developed by a new-born infant to enlargement of the thymus gland. Such opinions are based on the presence of a large upper mediastinal shadow, disregarding the fact that such a shadow is always present in well nourished new-born infants.

DR. MURRAY H. BASS: There is not much left to add. I feel strongly with DR. Mason that the symptomatology of the thymus gland and its relation to the roentgen ray is still in a state of great confusion. What DR. Schloss brought out about the shadow of the thymus being changed in a child according to its state of nutrition is of great importance. The first change that occurs in a case of malnutrition is that the thymus becomes small, so that after any prolonged illness a small thymus is usually found to be present. However, when death comes suddenly without prolonged illness, the thymus has not had time to atrophy and is therefore enlarged. This was well demonstrated during the World War, for many of the soldiers who were killed showed large thymus glands at autopsy. This, of course, did not mean that their sudden deaths were due to the enlargement of the thymus, but that their thymus glands were large at all times.

What we have heard is a real step in advance, and if we could get one definite method of roentgenography by which we could judge all cases, we would make great progress in our conception of the pathologic changes of the thymus.

DR. CHARLES HENDEE SMITH: It may be that the old saying applies that "none is so blind as he who will not see," but I cannot agree that an enlarged thymus accounts for many of the symptoms commonly attributed to it.

Dr. Pancoast's statement that the width of the shadow is no criterion as to size of the thymus is extremely important. While shadows are often seen with no symptoms, children with symptoms of tracheal pressure often show no increased width. This is especially true with the films taken with the child lying on its back. I have always felt that it was unfair to judge the thymic shadow except with the technic used for size of the heart, i. e., with the anterior part of the chest against the plate and the tube at a distance of 6 feet (182.9 cm.).

It may be, of course, that cases of enlarged thymus are more common in other cities than in New York. Dr. Schick has noted a great variation in diseases seen in this country and in the different cities of Europe.

What are the symptoms of thymus disease? It seems to me that we are at a loss to diagnose the condition in time in the cases in which sudden death is apparently attributable to this cause. I cannot convince myself that holding the breath, or spasms of rage, in older children is due to the condition of the thymus, or to recurrent colds, gastro-intestinal symptoms or all the other miscellaneous syndromes which are commonly ascribed to it. The stridor due to a soft larynx, described by Thompson as congenital stridor, is common enough and can have no relation to the thymus.

DR. EUGENE P. PENDERGRASS: In the work that Dr. Pancoast has presented he has outlined an effort which has been made to establish a technic by which one can, at least after some experience, be qualified in making a diagnosis of some obstructive lesion. As he brought out, in attempting to make a diagnosis of

enlarged thymus, he included an examination for all other possibilities of high obstruction. The reactions on the obstructive theory of the thymus have been confirmed by Dr. Jackson's work. Dr. Jackson has performed bronchoscopy in more than 300 patients in whom high obstructive lesions were present. He feels that the enlarged thymus does cause obstruction, asphyxiation and death, whether or not by encroachment on the lumen of the upper respiratory tract, I am not qualified to say. If one will read Noback's work in which he made careful studies on more than 400 cases of enlarged thymus glands, one will find almost every anomaly that can occur.

Another point is that in an infant, aged 3 months, Dr. Jackson states that the trachea is as easily collapsible as the rubber bulb on the medicine dropper. Through the apex of the thorax in such an infant the trachea, esophagus, nerves and all of the blood vessels pass; in a large group studied by Noback a portion of the thymus extended above the suprasternal notch. The anteroposterior diameter of the apex of the thorax in an infant is approximately 3 cm.

Dr. Pancoast has not tried to dignify the thymus as the major factor in the cause of death in status lymphaticus. The best work that I have read on this was done by Dr. Marine of New York, who believes that the enlargement of the thymus is not the cause of death in status lymphaticus, but that death is due to some constitutional defect. The roentgenologist, therefore, should not attempt to bring the thymus in as the main entity in status lymphaticus.

Dr. Mason brought up the point that Dr. Remer has stopped uterine bleeding by irradiating the spleen. Any one familiar with roentgen therapy knows that such things will happen. Possibly, irradiation over the spleen might cause some decrease in the size of the thymus.

We have performed bronchoscopy in a number of cases in which we could find no enlargement of the thymus because these infants had obstructive manifestations. In some of these cases there were evidences of recurrent laryngeal palsies and half a dozen had a prolapse of the soft tissues of the pharynx into the vestibule of the larynx.

I know that the question of when it is safe to give an anesthetic in cases of enlarged thymus is difficult. The roentgenologist should not be the court of last appeal except in stating that there is or is not roentgen evidence of enlargement of the thymus. One should not go further than that.

Dr. Smith brought up the question of the 6 foot films. We use 38 inches (95 cm.) because it is a convenient distance to make roentgenograms in the erect and horizontal postures. The percentage of error in children by the divergence of rays is relatively small.

ACADEMY OF MEDICINE OF CLEVELAND, PEDIATRIC SECTION

March 12, 1930

A. B. Grossman, M.D., *Secretary*

Celiac Disease. Dr. H. J. Gerstenberger.

An infant was presented who had marked symptoms of celiac disease and who had not improved until banana flour was added to the diet.

Tuberculous Meningitis. Dr. H. J. Gerstenberger.

A child, aged 3 years, was admitted to the Babies' and Children's Hospital in May, 1929. A diagnosis of tuberculous encephalitis, localized tuberculous meningitis and tuberculosis of the bone was made. The child is still a patient in the hospital and is improving on a high caloric diet and ultraviolet therapy.

A Case of Acrodynia. Dr. H. J. Gerstenberger.

A Case for Diagnosis. Dr. J. D. Pilcher.

A child who had been in the hospital three and a half months had intermittent high fever, extreme irritability and stiffness of the neck with increased reflexes, especially the patellar and achilles. All laboratory tests done, including urinalysis, blood culture, spinal fluid and blood counts, gave negative results. No definite diagnosis had been made.

Lobar Pneumonia. Dr. J. D. Pilcher.

A child was admitted to the hospital with an acute lobar pneumonia involving the whole upper lobe of the right lung. On recovery, it was observed that the heart was pulled to the affected side, probably owing to a shrinkage of the involved lung.

A Case of Aleukemic Leukemia. Dr. N. C. Wetzel.

Tuberculous Lung Cavitation. Dr. H. Reichle.

One case occurred in a child 4½ years old, another in a child 3½ years. If the cavities tend to disappear within a relatively short time, there is a good chance for recovery; if this takes a long time, there is danger of a bronchogenic distribution of the infection.

Encephalitis. Dr. L. P. Harsh.

The case presented was that of an infant who at 18 months of age developed pertussis of a severe form. During the acute stage, unusual irritative neurologic signs developed in the child and a diagnosis of encephalitis was made.

Von Jaksch's Anemia. Dr. G. R. Russell.

This infant with all the signs and symptoms of von Jaksch's anemia was treated by two intravenous and one intraperitoneal blood infusion, with a complete, uneventful recovery.

Multiple Neuritis. Dr. C. H. Vorr.

A child, aged 2, was admitted to the hospital because of a sudden inability to walk. Examination showed the disease limited to the peripheral nervous system. The etiology was not determined, but it was assumed to be infective rather than chemical in origin.

Diabetes Insipidus. Dr. L. R. Brigman.

This child had polydipsia and polyuria and drank enormous quantities of water. It was improved temporarily by daily hypodermic injections of gradually increasing doses of solution of pituitary.

Scurvy. Dr. C. L. Ruggles.

An infant had extreme pain over both thighs. It lay in the usual froglike posture. Roentgenograms of both femurs were positive for scurvy. The diet given was protein milk with orange juice, but the child did not react promptly to the specific treatment. No decided improvement was seen until one week after the treatment had been instituted.

Book Reviews

NURSING AND DISEASES OF SICK CHILDREN. A TEXT BOOK FOR NURSES AND WELFARE WORKERS. Edited by ALAN MONCRIEFF, M.D., B.S., M.R.C.P., London. Price, $4.50. Pp. 580, with 111 illustrations. In the American edition is an introduction by George R. Irving, M.D., of New York. New York: G. P. Putnam's Sons, 1930.

This book has been prepared to meet the great need for a comprehensive volume dealing with all the diseases of childhood written from and for the nurses' standpoint and based on the nurses' branch of medicine. It has been made as complete as possible, embracing a work of reference with a standard textbook for nurses specializing in child nursing.

In order that the special divisions of children's diseases might have the very best scientific treatment, the work is divided among four specialists, each an acknowledged master of his subject who has treated his own specialty in a scholarly way.

The book is divided into two parts: Part I, subdivided into three sections: General Considerations, General Nursing, General Surgical Nursing; Part II, Diseases of Children. The volume is dedicated "To the Nursing Staff of the Hospital for Sick Children, Great Ormond Street, Past, Present and Future." The writers of the four sections are members of the staff of this great hospital, and much of their material has been derived from its classrooms and wards. It is of interest to know that Great Ormond Street is in that part of London of which Dickens wrote, and that he was a loyal friend of the hospital in its early days.

Dr. Moncrieff and his co-writers emphasize throughout their writings the great importance of child nursing: "No branch of the art of nursing demanding more of its devotees in strength of character, intelligence and kindness of heart, as well as physical resilience."

The 111 illustrations add much to the helpfulness and interest of the book.

One cannot select a chapter or two chapters that are especially good or of especial importance—each chapter has its own place in the care of a child and is a masterpiece on its subject. Although the editor says that he and his co-authors have designed the book for nurses in training and as a reference book for the graduate nurse and welfare worker, it is written in such a simple, clear, concise, constructive style and is at the same time so thorough in its treatment that it is a wonderfully valuable book for any one to read and study and should be in every home. Mothers will find it most helpful and valuable in the care of their children. It should be in all Schools of Nursing and in the personal library of every one interested in or employed in child training. Its true value to the welfare of children will be realized the more it is read and studied.

GRUNDLAGEN DER ORTHODIAGRAPHISCHEN HERZGROZEN UND THORAXBREITENBEURTEILUNG IM KINDESALTER. By DR. OSKAR KIRSCH. Price, 7.20 marks. Pp. 110, with 24 tables. Berlin: S. Karger, 1929.

For many years the roentgenologists have been using 50 per cent as the limit of normal variation for the thoracic heart index. On the other hand, if the transverse diameter of the heart as obtained from a plate taken at a distance of 6 feet is 51 per cent or more of the transverse width of the thorax at its widest level (the upper part of the diaphragm), the size of the heart is considered abnormal. The author has attempted to answer these questions: How far can this index be used for diagnosis, and how variable is the relationship between the size and shape of the heart to the chest in normal children? He has perfected the technic of orthodiagraphy for use in infants as well as in children. Further-

more, he has correlated the transverse diameter of the heart in 127 children between the ages of 2 and 15 years, with the age, the sex, the height, the weight and the diameter of the thorax. He has also carefully measured the various dimensions of the heart and correlated them with each other and also with the thorax. He has shown that it is not a simple task to establish an index or formula of the normal heart for the different ages because of the great variation in the size and shape of the heart and chest of normal children.

The chapter on the asthenic, the infantile and other atypical types is especially comprehensive. The author should be particularly commended for the publication of his original data, a matter which many writers neglect to include. He gives the means of the thoracic heart index as 49.68 per cent for boys and 49.77 per cent for girls. The standard deviation is 2.73 and 2.49, respectively. The combined means of all the cases is 49.72 per cent, with a standard deviation of 2.65. Unfortunately, the number of cases for each age is very small. Another question which comes to the mind of the reviewer is whether the method used, though theoretically more accurate than the usual stereoscopic examination of the heart at a distance of 6 feet, will ever be of practical use in routine examinations. It is extremely difficult to get a child to remain still for five minutes, and yet any movement of the body will make the error considerable. Moreover, a comparison of Kirsch's figures with those of Lincoln, who used the ordinary method, shows practically the same means. Here the standard deviation is not any higher than that given in the present work. In this monograph the author has accumulated a mass of important material, not only for the roentgenologists, but also for the pediatricians and the cardiologists.

La dyspepsie transitoire des nourissons. Alfonso G. Alarcón. Pp. 140, with 5 illustrations. Paris: J. B. Baillière et fils., 1929.

The author believes that the so-called transitory dyspepsia of the infant is really a symptom of vagotonia. The characteristic symptoms of spasticity, colic, vomiting, hyperexcitability and pylorospasm are fully described in the initial chapters. The following five chapters are devoted to the physiology and pathologic changes of the condition. The final chapters consider a differential diagnosis and treatment. The book is interesting and well written.

Medical and Surgical Year Book. Physicians Hospital of Plattsburgh. Price, $3.50. Pp. 322, with 71 illustrations. Plattsburgh, N. Y.: William H. Miner Foundation, 1930.

This volume contains the collected papers of twenty-two invitational lectures on cardiac conditions, the first Beaumont lecture and fourteen papers on general medicine from the staff of the Physicians Hospital.

Directory of Pediatric Societies

INTERNATIONAL

International Pediatric Congress

Prof. I. Jundell, Artillerigatan 23, Stockholm, Sweden.
Place: Stockholm. Time: Aug. 17-20, 1930.

NATIONAL

American Medical Association, Scientific Assembly, Section on Diseases of Children

Chairman: Dr. C. A. Aldrich, 545 Lincoln Ave., Winnetka, Ill.
Secretary: Dr. Alfred A. Walker, Highland Plaza Apartments, Birmingham, Ala.
Place: Philadelphia. Time: 1931.

American Academy of Pediatrics

President: Dr. I. A. Abt, 104 S. Michigan Ave., Chicago.
Secretary: Dr. C. G. Grulee, 310 S. Michigan Ave., Chicago.

American Child Health Association

President: Hon. Herbert Hoover, 370 7th Ave., New York.
Secretary: Dr. Philip Van Ingen, 370 7th Ave., New York.

American Pediatric Society

President: Dr. Philip Van Ingen, 125 E. 71st St., New York.
Secretary-Treasurer: Dr. Howard Childs Carpenter, 1805 Spruce St., Philadelphia.
Place: New York.

Association of American Teachers of the Diseases of Children

President: Dr. Lawrence T. Royster, State Board of Health, University, Va.
Secretary: Dr. Ralph M. Tyson, 334 S. 21st St., Philadelphia.

Children's Hospital Association of America

President: Dr. Howard Childs Carpenter, 1805 Spruce St., Philadelphia.
Secretary-Treasurer: Miss Bena M. Henderson, Milwaukee Children's Hospital, Milwaukee.
Place: New Orleans, La. Time: October, 1930.

Canadian Society for the Study of Diseases of Children

President: Dr. E. A. Morgan, 160 Bloor St., Toronto, Ont.
Secretary-Treasurer: Dr. George E. Smith, 244 Bloor St., W., Toronto, Ont.

SECTIONAL

Central States Pediatric Society

President: Dr. Edward Clay Mitchell, 1073 Madison Ave., Memphis, Tenn.
Secretary: Dr. A. H. Parmelee, 310 S. Michigan Blvd., Chicago.
Place: Memphis, Tenn. Time: Fall, 1930.

Southern Medical Association, Section on Pediatrics

Chairman: Dr. H. Leslie Moore, 1717 Pacific Ave., Dallas, Texas.
Secretary: Dr. Ludo von Meysenbug, 3501 Prytania St., New Orleans, La.
Place: Louisville, Ky.: November, 1930.

STATE

Alabama Pediatric Society

President: Dr. Hughes Kennedy, Jr., Highland Plaza Apts., Birmingham.
Secretary-Treasurer: Dr. John W. Simpson, 1117 S. 22nd St., Birmingham.

Georgia Pediatric Society

President: Dr. W. N. Adkins, Medical Arts Bldg., Atlanta.
Secretary-Treasurer: Dr. E. N. Gleaton, 212 E. Gaston St., Savannah.

Louisiana State Pediatric Society

President: Dr. R. A. Strong, 1551 Canal St., New Orleans.
Secretary-Treasurer: Dr. Suzanne Schaeffer, Chailie Bldg., New Orleans.

Oklahoma State Pediatric Society

President: Dr. Carroll M. Pounders, 210 W. 10th St., Oklahoma City.
Secretary: Dr. C. E. Bradey, Medical Arts Bldg., Tulsa.
Place: Oklahoma City. Time: May, 1931.

South Carolina Pediatric Society

President: Dr. M. W. Beach, 126 Meeting St., Charleston.
Secretary-Treasurer: Dr. Julian P. Price, The McLeod Infirmary, Florence.

Texas Pediatric Society

President: Dr. L. O. Godley, 600 W. 10th St., Fort Worth.
Secretary-Treasurer: Dr. John G. Young, 3930 McKinney Ave., Dallas.

Virginia Pediatric Society

President: Dr. Franklin D. Wilson, 136 York St., Norfolk.
Secretary: Dr. J. B. Stone, 2042 Park Ave., Richmond.

LOCAL

Academy of Medicine of Cleveland, Pediatric Section

Chairman: Dr. John Toomey, Cleveland City Hospital, Cleveland.
Secretary: Dr. A. B. Grossman, 7016 Euclid Ave., Cleveland.
Place: 2009 Adelbert Road. Time: Four meetings, from September to May.

Academy of Medicine, Toronto, Section of Pediatrics

President: Dr. Gladys Boyd, 56 DeLisle St., Toronto.
Secretary: Dr. Lawrence Murray, 1870 Bloor St., West, Toronto.
Time: November 17, December 15, February 16 and March 15.

Bronx Pediatric Society

President: Dr. David I. Frey, 2065 Grand Concourse, New York.
Secretary: Dr. H. M. Eisenoff, 1018 E. 163rd St., New York.
Place: Concourse Plaza, 161st St. and Grand Concourse. Time: Second Wednesday of each month, except June, July, August and September.

Brooklyn Pediatric Society

President: Dr. Joseph F. Paulonis, 1357 Bushwick Ave., Brooklyn.
Secretary: Dr. Irwin Schiff, 658 Eastern Parkway, Brooklyn.
Place: Kings County Medical Society Bldg. Time: Last Wednesday of each month, except June, July and August.

Central New York Pediatric Club

President: Dr. Frank Vander Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Fourth Thursday of October, January and April.

Chicago Pediatric Society

President: Dr. Arthur H. Parmelee, 310 S. Michigan Blvd., Chicago.
Secretary: Dr. Bert I. Beverly, 8 S. Michigan Ave., Chicago.
Place: City Club. Time: Third Tuesday of each month.

Detroit Pediatric Society

President: Dr. Wyman C. C. Cole, 2970 W. Grand Blvd., Detroit.
Secretary: Dr. Charles A. Wilson, 71 E. Perry St., Detroit.
Place: Children's Hospital of Michigan. Time: No fixed date; approximately once a month.

Fulton County Medical Society, Pediatric Section (Atlanta, Ga.)

Chairman: Dr. Lee Bivings, Exchange Bldg., Atlanta.
Secretary: Dr. William Kiser, Medical Arts Bldg., Atlanta.
Place: Academy of Medicine, 32 Howard St. Time: Second Thursday of each month from October to April, 8 p. m.

Memphis Pediatric Society

President: Dr. G. J. Levy, 899 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. W. R. Graves, 1024 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month.

Milwaukee Pediatric Society

President: Dr. M. G. Peterman, 167 17th St., Milwaukee.
Secretary: Dr. F. R. Janney, 418 E. North Ave., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

Nebraska Pediatric Society

President: Dr. H. B. Hamilton, 434 Aquila Court Bldg., Omaha.
Secretary: Dr. George L. Clark, 1817 Vinton St., Omaha.
Place: As announced by committee. Time: Second Thursday of each month from October to June, inclusive, 6 p. m.

New England Pediatric Society

President: Dr. Grover F. Powers, New Haven, Conn.
Secretary: Dr. Gerald Hoeffel, 319 Longwood Ave., Boston.
Place: Boston Medical Library. Time: October, January and March.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. Hugh Chaplin, 39 E. 75th St., New York.
Secretary: Dr. John P. Caffey, Babies' Hospital, 167th Street and Broadway, New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

North Pacific Pediatric Society

President: Dr. W. F. Patrick, Medical Arts Bldg., Portland, Ore.
Secretary: Dr. L. Howard Smith, Medical Arts Bldg., Portland, Ore.

Northern California Pediatric Society

President: Dr. Edward B. Shaw, 384 Post St., San Francisco.
Secretary-Treasurer: Dr. Lloyd Hardgrave, 384 Post St., San Francisco.
Place: Various teaching schools. Time: Monthly.

Northwestern Pediatric Society

President: Dr. E. S. Platou, 730 La Salle Bldg., Minneapolis.
Secretary: Dr. F. G. Hedenstrom, 218 Lowry Bldg., St. Paul.
Place: University Campus and Rochester, Minn. Time: Winter, Spring, Summer, Fall.

Philadelphia Pediatric Society

President: Dr. Ralph M. Tyson, 334 S. 21st St., Philadelphia.
Secretary: Dr. John D. Donnelly, 115 Bryn Mawr Ave., Bala-Cynwyd, Pa.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to June, inclusive.

Pittsburgh Pediatric Society

President: Dr. David H. Boyd, 200, 9th St., Pittsburgh.
Secretary: Dr. Theodore O. Elterich, Highland Bldg., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate months from October to April, inclusive.

Richmond Pediatric Society

President: Dr. Basil B. Jones, 2618 Grove Ave., Richmond, Va.
Secretary-Treasurer: Dr. John S. Weitzel, 3103 W. Franklin St., Richmond, Va.
Place: Westmoreland Club, 601 E. Grace St. Time: First Thursday of each month (other than during the summer).

Rochester Pediatric Society

President: Dr. John Aikman, 184 Alexander St., Rochester, N. Y.
Secretary: Dr. Howard F. Rowley, 176 S. Goodman St., Rochester, N. Y.
Place: Arranged by program committee. Time: First Friday of each month from October to May.

Rocky Mountain Pediatric Society

President: Dr. Bernard C. Dorset, 1612 Tremont St., Denver.
Secretary-Treasurer: Dr. Wilford W. Barber, 227, 16th St., Denver.
Place: Children's Hospital, Denver. Time: Third Saturday of each month from September to May, inclusive, 2:30 p. m.

St. Louis Pediatric Society

President: Dr. Gustave Lippmann, 3720 Washington Blvd., St. Louis.
Secretary-Treasurer: Dr. Katherine Bain, 3720 Washington Blvd., St. Louis.
Place: St. Louis Children's Hospital. Time: At least once a year and contingent thereafter on the arrangement of a suitable program.

Seattle Pediatric Society

President: Dr. Vernon W. Spickard, Cobb Bldg., Seattle.
Secretary: Dr. Raymond H. Somers, Cobb Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, 7 p. m.

Southwestern Pediatric Society

President: Dr. William S. Bowers, 1136 W. 6th St., Los Angeles.
Secretary: Dr. Fred L. Glascock, 1136 W. 6th St., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. W. D. Lyon, 101 S. Balch St., Akron, Ohio.
Secretary: Dr. John P. Parsons, 320 S. Division St., Ann Arbor, Mich.
Place: Ann Arbor, Mich. Time: November 14 and 15, 1930.